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NEWS 21	Jun 10	PCTFULL has been reloaded

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=> s immunoglobulin light chain
L1       14222 IMMUNOGLOBULIN LIGHT CHAIN

=> s l1 and soluble
L2         350 L1 AND SOLUBLE

=> s l2 and peptide
L3          77 L2 AND PEPTIDE

=> s l3 and inhibit binding
L4           0 L3 AND INHIBIT BINDING

=> s l3 and mast cell
   4 FILES SEARCHED...
L5           0 L3 AND MAST CELL

=> dup remove l3
PROCESSING COMPLETED FOR L3
L6           49 DUP REMOVE L3 (28 DUPLICATES REMOVED)

=> s l6 and mimetic
L7           0 L6 AND MIMETIC

=> d l6 1-49 cbib abs

L6   ANSWER 1 OF 49  CAPLUS  COPYRIGHT 2002 ACS
2001:903933   Document No. 136:36341  Single-chain T cell antigen receptor
     fusion proteins.  Weidanz, Jon A.; Card, Kimberlyn F.; Wong, Hing C.
     (Sunol Molecular Corporation, USA).  PCT Int. Appl. WO 2001093913 A2
     20011213, 66 pp.  DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA,
     BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES,
     FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
     LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL,
     PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN,
     YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF,
     CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML,
     MR, NE, NL, PT, SE, SN, TD, TG, TR.  (English).  CODEN: PIXXD2.
     APPLICATION: WO 2001-US18145 20010605.  PRIORITY: US 2000-PV209536
     20000605.
AB   The authors disclose the prepn. and characterization of single-chain T
     cell receptor fusion proteins engineered to recognize target antigen in a
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functionally bispecific nature. In one example, the authors prep. a fusion of human interleukin-2 with a single-chain TCR directed to an HLA-A2-restricted epitope of p53. After **peptide** loading to an HLA-A2+ B-cell line, the fusion protein promoted cell-cell conjugation with T-cells.

L6 ANSWER 2 OF 49 CAPLUS COPYRIGHT 2002 ACS

2001:636109 Document No. 135:225860 Humanized antibodies that sequester amyloid .beta. (A.beta.) **peptide**. Holtzman, David M.; Demattos, Ronald; Bales, Kelly R.; Paul, Steven M.; Tsurushita, Naoya; Vasquez, Maximiliano (Washington University, USA; Eli Lilly and Company). PCT Int. Appl. WO 2001062801 A2 20010830, 63 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US6191 20010226. PRIORITY: US 2000-PV184601 20000224; US 2000-PV254465 20001208; US 2000-PV254498 20001208.

AB A method to treat conditions characterized by formation of amyloid plaques both prophylactically and therapeutically is described. The method employs humanized antibodies which sequester **sol**. A.beta. **peptide** from human biol. fluids or which preferably specifically bind an epitope contained within position 13-28 of the amyloid beta **peptide** A.beta.. The humanized antibodies and fragments are useful for preventing and treating conditions assocd. with A.beta., such as Alzheimer's disease, Down's syndrome, cerebral amyloid angiopathy, and cognitive decline.

L6 ANSWER 3 OF 49 CAPLUS COPYRIGHT 2002 ACS

2001:472757 Document No. 135:75753 **Soluble** interleukin-20 receptor. Foster, Donald C.; Xu, Wenfeng; Madden, Karen L.; Kelly, James D.; Sprecher, Cindy A.; Brandt, Cameron S.; Rixon, Mark W.; Presnell, Scott R.; Fox, Brian A. (Zymogenetics, Inc., USA). PCT Int. Appl. WO 2001046232 A2 20010628, 118 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US35307 20001222. PRIORITY: US 1999-471774 19991223; US 2000-PV213416 20000622.

AB A **sol**. receptor to IL-20 having two polypeptide subunits, IL-20RA (formerly called ZcytoR7) and IL-20RB (formerly called DIRS1). The two subunits are preferably linked together. In one embodiment one subunit is fused to the const. region of the light chain of an Ig, and the other subunit is fused to the const. region of the heavy chain of the Ig. The light chain and the heavy chain are connected via a disulfide bond.

L6 ANSWER 4 OF 49 CAPLUS COPYRIGHT 2002 ACS

2001:435310 Document No. 135:41773 Use of multiple recombination sites with unique specificity in recombinational cloning. Cheo, David; Brasch, Michael A.; Temple, Gary F.; Hartley, James L.; Byrd, Devon R. N. (USA). PCT Int. Appl. WO 2001042509 A1 20010614, 357 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,

TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US33546 20001211. PRIORITY: US 1999-PV169983 19991210; US 2000-PV188020 20000309.

AB The present invention provides compns. and methods for recombinational cloning. The compns. include vectors having multiple recombination sites with unique specificity. The methods permit the simultaneous cloning of two or more different nucleic acid mols. In some embodiments the mols. are fused together while in other embodiments the mols. are inserted into distinct sites in a vector. The invention also generally provides for linking or joining through recombination a no. of mols. and/or compds. (e.g., chem. compds., drugs, proteins or **peptides**, lipids, nucleic acids, carbohydrates, etc.) which may be the same or different. Such mols. and/or compds. or combinations of such mols. and/or compds. can also be bound through recombination to various structures or supports according to the invention.

L6 ANSWER 5 OF 49 CAPLUS COPYRIGHT 2002 ACS

2001:645629 Document No. 135:225871 Anti-TNF.alpha. antibodies and assays employing anti-TNF.alpha. antibodies. Le, Junming; Vilcek, Jan; Dadonna, Peter; Ghrayeb, John; Knight, David; Siegel, Scott A. (New York University Medical Center, USA; Centocor, Inc.). U.S. US 6284471 B1 20010904, 87 pp., Cont.-in-part of U.S. Ser. No. 10,406, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1994-192093 19940204. PRIORITY: US 1991-670827 19910318; US 1992-853606 19920318; US 1992-943852 19920911; US 1993-10406 19930129; US 1993-13413 19930202.

AB Anti-TNF antibodies and anti-TNF **peptides**, specific for tumor necrosis factor (TNF) are useful for in vivo diagnosis and therapy of a no. of TNF-mediated pathologies and conditions, as well as polynucleotides coding for anti-TNF murine and chimeric antibodies, **peptides**, methods of making and using the antibody or **peptides** in immunoassays and immuno-therapeutic approaches are provided, where the anti-TNF **peptide** is selected from a **sol**. portion of TNF receptor, an anti-TNF antibody or structural analog thereof. The TNF-mediated diseases include bacterial, vial or parasitic infections, chronic inflammatory diseases, autoimmune diseases, malignancies, and/or neurodegenerative diseases.

L6 ANSWER 6 OF 49 MEDLINE

2001678557 Document Number: 21571705. PubMed ID: 11714806. Surrogate light chain-mediated interaction of a **soluble** pre-B cell receptor with adherent cell lines. Bradl H; Jack H M. (Division of Molecular Immunology, Department of Internal Medicine III, Nikolaus-Fiebiger Center, University of Erlangen-Nurnberg, Erlangen, Germany.) JOURNAL OF IMMUNOLOGY, (2001 Dec 1) 167 (11) 6403-11. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Signals initiated by the precursor B cell receptor (pre-BCR) are critical for B cell progenitors to mature into precursor B cells. The pre-BCR consists of a homodimer of microH chains, the covalently associated surrogate L (SL) chain composed of VpreB and lambda5, and the transmembrane signal molecules Ig(alpha) and Igbeta. One way to explain how maturation signals are initiated in late progenitor B cells is that the pre-BCR is transported to the cell surface and interacts from there with a ligand on stroma cells. To address this hypothesis, we first produced **soluble** Fab-like pre-BCR and BCR fragments, as well as SL chain, in baculovirus-infected insect cells. Flow cytometry revealed that, in contrast to Fab-like BCR fragments, the **soluble** pre-BCR binds to the surface of stroma and several other adherent cell lines, but not to B and T lymphoid suspension cells. The specific binding of the **soluble** pre-BCR to stroma cells is saturable, sensitive to trypsin digestion, and not dependent on bivalent cations. The binding of pre-BCR

seems to be independent of the H chain of IgM (microH chain), because SL chain alone was able to interact with stroma cells. Finally, **soluble** pre-BCR specifically precipitated a 135-kDa protein from ST2 cells. These findings not only demonstrate for the first time the capacity of a pre-BCR to specifically bind to a structure on the surface of adherent cells, but also suggest that the pre-BCR interacts via its SL chain with a putative ligand on stroma cells.

L6 ANSWER 7 OF 49 MEDLINE

2001385330 Document Number: 21332773. PubMed ID: 11439026. Building novel binding ligands to B7.1 and B7.2 based on human antibody single variable light chain domains. van den Beucken T; van Neer N; Sablon E; Desmet J; Celis L; Hoogenboom H R; Hufton S E. (Dyax B.V., Provisorium, Maastricht, 6202 AZ, The Netherlands.) JOURNAL OF MOLECULAR BIOLOGY, (2001 Jul 13) 310 (3) 591-601. Journal code: 2985088R. ISSN: 0022-2836. Pub. country: England: United Kingdom. Language: English.

AB Ligands specific for B7.1 (CD80) and B7.2 (CD86) have applications in disease indications that require inhibition of T-cell activity. As we observed significant sequence and structural similarity between the B7-binding ligand, cytotoxic T-lymphocyte associated protein-4 (CTLA-4), and antibody variable light chain domains (VLs), we have explored the possibilities of making novel B7 binding molecules based on single VL domains.We first describe the "rational" design and construction of a VL/CTLA-4 hybrid molecule in which we have grafted both the CDR1 and CDR3-like loops of CTLA-4 onto a single VL light chain, at sites determined by sequence and structure-based alignment. This molecule was secreted as a **soluble** product from Escherichia coli, but did not show any binding to B7.1 and B7.2. In a second approach we constructed a VL library in which human VL genes derived from B-cells were spiked with the CDR3-like loop of CTLA-4 and further diversified by DNA shuffling. This library was displayed on phage, and after selection gave B7.1 binding ligands which competed with CTLA-4. In order to evaluate the possible general utility of VL domains as binding ligands, we have constructed a non-biased VL library. From this DNA-shuffled human VL library we have selected single VL domains specific for B7.1, B7.2 or human IgG. Two B7.1-specific VL ligands and one B7.2-specific VL ligand showed competition with CTLA-4. One candidate VL domain-specific for B7.1 was affinity matured by simultaneous randomisation of all CDR loops using DNA shuffling with degenerate CDR-spiking oligonucleotides. From this library, a single VL domain with affinity of 191 nM for B7.1 was obtained, which also showed binding to B7.1 in situ. This VL had mutations in CDR1 and CDR3, indicating that antigen recognition for this single VL is most likely mediated by the same regions as in the VL domain of whole antibodies.The B7.1 and B7.2-specific VL domains described in this study may form the basis of a new family of immunomodulatory recombinant molecules. Furthermore, our studies suggest that it is feasible to create specific single VL domains to diverse targets as is the case for single VH domains.

L6 ANSWER 8 OF 49 SCISEARCH COPYRIGHT 2002 ISI (R)

2001:899392 The Genuine Article (R) Number: 489HQ. Evidence that supramolecular Congo red is the sole ligation form of this dye for L chain lambda derived amyloid proteins. Rybarska J (Reprint); Piekarska B; Stopa B; Zemanek G; Konieczny L; Nowak M; Krol M; Roterman I; Szymczakiewicz-Multanowska A. Jagiellonian Univ, Coll Med, Isnt Med Biochem, PL-31034 Krakow, Poland; Jagiellonian Univ, Coll Med, Dept Biostat & Med Informat, PL-31034 Krakow, Poland; Jagiellonian Univ, Coll Med, Dept Nephrol, PL-31034 Krakow, Poland. FOLIA HISTOCHEMICA ET CYTOBIOLOGICA (NOV 2001) Vol. 39, No. 4, pp. 307-314. Publisher: POLISH HISTOCHEMICAL CYTOCHEMICAL SOC. VESALUIS MEDICAL PUBLISHING, WISLISKO 1, 31-538 KRAKOW, POLAND. ISSN: 0015-5586. Pub. country: Poland. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The mechanism of Congo red binding to amyloid protein was studied in order to establish which of two structural dye versions present in water solutions-unimolecular and supramolecular-represent its actual ligation form. Immunoglobulin L chain lambda of amyloidogenic nature, expressed by Congo red binding and easy gel formation, was used as the model amyloid protein. Congo red was coassembled with rhodamine B. designed to be a marker of the Congo red micellar organisation in complexation with protein. The particular suitability of rhodamine B for this role results from significant difference in its binding affinity to Congo red and to protein. It associates readily with Congo red, becoming incorporated into its micellar organisation, but as homogenous dye it shows an almost complete inability to bind to protein. In view of these properties, Congo red was used as a vehicle to draw rhodamine B into complexation with protein, at the same time supplying evidence of its supramolecular ligation form. The results show that both **soluble** amyloid precursor L chain and the derived gel material attach rhodamine B coassembled with Congo red but not the homogenous rhodamine B. Despite its dynamic, supramolecular character, Congo red participates in complexation with amyloid proteins as an integral ligand unit.

L6 ANSWER 9 OF 49 MEDLINE

2001343268 Document Number: 21299533. PubMed ID: 11406160. Interaction of the octapeptide angiotensin II with a high-affinity single-chain Fv and with **peptides** derived from the antibody paratope. Cohen P; Laune D; Teulon I; Combes T; Pugniere M; Badouaille G; Granier C; Mani J C; Simon D. (Department of Immunology/Oncology, Sanofi-Synthelabo, 371 rue du Professeur Blayac, 34184 Montpellier Cedex 4, France.) JOURNAL OF IMMUNOLOGICAL METHODS, (2001 Aug 1) 254 (1-2) 147-60. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB The amino-acid sequence of the very high-affinity anti-angiotensin II monoclonal antibody 4D8 was predicted from the nucleotide sequence of the heavy and light chain variable genes. The single-chain variable fragment (scFv) was constructed and expressed in Escherichia coli as a **soluble** protein and at the surface of the filamentous M13 phage and was compared with the full-length antibody (Ab). The scFv showed the same specificity profile and affinity constant as the intact antibody (5.0x10(10) and 8.0x10(10) M(-1), respectively, by Scatchard analysis). Several **peptides** from the set of overlapping dodecapeptides covering the variable domains of 4D8 mAb were found to specifically bind biotinylated angiotensin II: **peptides** from the L1, L2, L3 and H1 regions had the strongest capacity to bind the antigen.

L6 ANSWER 10 OF 49 MEDLINE

2001155428 Document Number: 21108696. PubMed ID: 11161238. Isolation of an IgG anti-B from a human Fab-phage display library. Chang T Y; Siegel D L. (Department of Pathology and Laboratory Medicine, University of Rochester, Rochester, New York, USA.) TRANSFUSION, (2001 Jan) 41 (1) 6-12. Journal code: 0417360. ISSN: 0041-1132. Pub. country: United States. Language: English.

AB BACKGROUND: ABO incompatibility is a common cause for mild hemolysis in the newborn, ranging from 1 in 30 to 1 in 150 births. Fortunately, hemolysis requiring transfusion is rare and restricted to blood group O mothers, because blood group A and B individuals make poor IgG anti-B and anti-A responses. No human IgG ABO antibody sequences have been reported, in part because of the difficulty in obtaining human IgG hybridomas. Phage-display technology may be able to circumvent these difficulties, but its application to carbohydrate antigens is poorly studied. STUDY DESIGN AND METHODS: A human IgG1 phage-display Fab library was constructed from splenocytes derived from a nonhyperimmunized blood group O person, and panned against group B RBCs. RESULTS: After five rounds of panning, essentially all phage bound to group B RBCs. Nucleotide sequence analysis of a single monoclonal IgG1lambda phage, FB5.7, revealed a highly mutated

VH4 family heavy chain, and a nearly germline VL7 family lambda light chain. The Fab agglutinated group B, but not group A, random-donor RBCs. However, group B ELISA reactivity could be inhibited by **soluble** B-trisaccharide, **soluble** A-trisaccharide, galactose, and N-acetyl galactosamine. Similarly, galactose and N-acetyl galactosamine were able to inhibit group B RBC agglutination. CONCLUSION: FB5.7 is the first human IgG ABO MoAb described. Alhough it behaves serologically like a group B-specific antibody, it demonstrates interaction with both the A and B epitopes. Phage-display technology can be used to better define the relationship between antibody genotype and phenotype in anti-carbohydrate responses in nonhyperimmunized hosts, and thus to improve our understanding of the composition of the antibody repertoire.

L6 ANSWER 11 OF 49 CAPLUS COPYRIGHT 2002 ACS

2000:666777 Document No. 133:251277 A novel chimeric protein for prevention and treatment of HIV infection. Berger, Edward A.; Del Castillo, Christie M. (United States of America, Department of Health & Human Services, the Nat, USA). PCT Int. Appl. WO 2000055207 A1 20000921, 55 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US6946 20000316. PRIORITY: US 1999-PV124681 19990316.

AB This invention relates to bispecific fusion proteins effective in viral neutralization. More specifically, such proteins have two different binding domains, an inducing-binding domain and an induced-binding domain, functionally linked by a **peptide** linker. Such proteins, nucleic acid mols. encoding them, and their prodn. and use in preventing or treating viral infections are provided. One prototypical bispecific fusion protein is sCD4-scFv(17b), in which a **sol**. CD4 fragment (contg. domains D1 and D2) is fused to a single chain Fv portion of antibody 17b via a linker.

L6 ANSWER 12 OF 49 CAPLUS COPYRIGHT 2002 ACS

2000:98610 Document No. 132:165123 Heterominibodies. Kufer, Peter; Dreier, Torsten; Baeuerle, Patrick A.; Borschert, Katrin; Zettl, Florian (Micromet Gesellschaft Fur Biomedizinische Forschung m.b.H., Germany). PCT Int. Appl. WO 2000006605 A2 20000210, 166 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP5416 19990728. PRIORITY: EP 1998-114082 19980728.

AB The present invention relates to a multifunctional compd., produceable in a mammalian host cell as a secretable and fully functional heterodimer of two polypeptide chains, wherein one of said polypeptide chains comprises, as the only const. region domain of an Ig heavy chain the CH1-domain and the other polypeptide chain comprises the const. CL-domain of an **Ig light chain**, wherein said polypeptide chains further comprise, fused to said const. region domains at least two (poly)**peptides** having different receptor or ligand functions, wherein further at least two of said different (poly)**peptides** lack an intrinsic affinity for one another and wherein said polypeptide chains are linked via said const. domains. Preferably, said domains, having receptor or ligand function, are in the format of a scFv-fragment and/or are immuno-modulating effector mols. Most preferably, said

scFV-fragment comprises the VH and the VL regions of the murine anti-17-1A antibody M79, the VH and the VL regions of the anti-Lewis Y antibody, as shown in Fig. 6, or the VH and the VL regions of the anti-CD3 antibody TR66 and/or said immuno-modulating effector mol. comprises cytokines or chemokines. Furthermore, the present invention relates to polynucleotides encoding said polypeptide chains as well as vectors comprising said polynucleotides and host cells transformed therewith as well as the use of the above embodiments for the prodn. of said multifunctional compds. In addn., pharmaceutical and diagnostic compns. are provided, comprising any of the afore-described multifunctional compds., polynucleotides or vectors. Described is also the use of the afore-mentioned multifunctional compd. for preventing and/or treating malignant cell growth, related to malignancies of hemopoietic cells or to solid tumors. Thus, heterominibody comprising (1) scFv of murine anti-17-1A antibody M79 and human CD80 extracellular domain, (2) scFv of anti-Lewis Y and CD80 extracellular domain, (3) M79scFv and CD54, (4) M79scFv and CD58, (5) M79scFv and CD86, (6) M79scFv and anti-CD3 scFv and CD80, (7) anti-EpCAM (HD70scFv) linked to GM-CSF and anti-EpCAM (HD70scFv) linked to interleukin 2 were prepd. and tested.

L6 ANSWER 13 OF 49 CAPLUS COPYRIGHT 2002 ACS

2000:769010 Document No. 133:334053 Preparation and characterization of **sol**. multivalent chimeric TCR/Ig or MHC/Ig molecular complexes to analyze and modulate antigen-specific T cell-dependent immune responses. Schneck, Jonathan; O'Herrin, Sean; Lebowitz, Michael S.; Hamad, Abdel (The Johns Hopkins University, USA). U.S. US 6140113 A 20001031, 41 pp., Cont.-in-part of U.S. 6,015,884. (English). CODEN: USXXAM. APPLICATION: US 1998-63276 19980421. PRIORITY: US 1996-PV14367 19960328; US 1997-828712 19970328.

AB **Sol**. multivalent chimeric TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses are described. The mol. complexes comprise extracellular domains of transmembrane heterodimeric proteins, particularly T cell receptor and major histocompatibility complex proteins, which are covalently linked to the heavy and light chains of Ig mols. to provide **sol**. multivalent mol. complexes with high affinity for their cognate ligands. Studies of the affinity and binding specificity of these multivalent chimeric TCR/Ig or MHC/Ig mols. to antigenic **peptides** are reported. The mol. complexes can be used, inter alia, to detect and regulate antigen-specific T cells and as therapeutic agents for treating disorders involving immune system regulation, such as allergies, autoimmune diseases, tumors, infections, and transplant rejection.

L6 ANSWER 14 OF 49 CAPLUS COPYRIGHT 2002 ACS

2000:396929 Document No. 133:148904 Antiferritin single-chain Fv fragment is a functional protein with properties of a partially structured state: Comparison with the completely folded VL domain. Martsev, Sergey P.; Chumanevich, Alexander A.; Vlasov, Alexander P.; Dubnovitsky, Anatoly P.; Tsybovsky, Yaroslav I.; Deyev, Sergey M.; Cozzi, Anna; Arosio, Paolo; Kravchuk, Zinaida I. (Institute of Bio-Organic Chemistry, Minsk, 220141, Belarus). Biochemistry, 39(27), 8047-8057 (English) 2000. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.

AB Differential scanning calorimetry and spectroscopic probes were applied to study folding and stability of the single-chain Fv fragment (scFv) of the anti-human ferritin antibody F11 and its isolated variable light-chain (VL) domain. The scFv fragment followed variable heavy-chain domain (VH)-linker-VL orientation and contained (Gly4Ser)3 linker **peptide** . The two proteins were produced in Escherichia coli and refolded from denaturant-solubilized inclusion bodies. The isolated VL domain demonstrated a typical Ig fold with well-defined secondary and tertiary structure and was capable of binding human ferritin with Ka = 1.8.times.107 M-1, .apprx.1/30 of the affinity of the parent F11 antibody. Involvement of this VL domain into the two-domain scFv fragment yielded a

distorted secondary and significantly destabilized tertiary structure in which neither of the two constituent domains attained complete folding. The thermal unfolding enthalpy of scFv F11 at pH 7.0 was as low as 5.0 J.cntdot.g-1 vs. 16.3 J.cntdot.g-1 obtained for the VL domain and 24.7 J.cntdot.g-1 for the parent F11 antibody (mouse IgG2a subclass). Intrinsic fluorescence and near-UV circular dichroic (CD) spectra, and binding of the hydrophobic probe 8-anilino-1-naphthalene sulfonate, confirmed partial loss of tertiary interactions in scFv. The spectroscopic and calorimetric properties of scFv F11 under physiol. conditions are consistent with a model of a partially structured state with a distorted .beta.-sheet as a secondary structure and partial loss of tertiary interactions, which closely resembles the alternatively folded A-state adopted by an Ig at pH 2-3. However, scFv F11 demonstrated only an .apprx.4-fold decrease in the antigen-binding affinity (Ka = 1.3.times.108 M-1) vs. the parent F11 antibody. The scFv fragment F11 provides the first description of a functional protein trapped under physiol. conditions in a partially structured state. This state is either close to the native one in the antigen-binding affinity or, alternatively, initial weak binding of the antigenic epitope induces folding of scFv F11 into a more structured conformation that generates relatively high affinity.

L6 ANSWER 15 OF 49 CAPLUS COPYRIGHT 2002 ACS

2000:492801 Document No. 133:277698 The Protofilament Substructure of Amyloid Fibrils. Serpell, Louise C.; Sunde, Margaret; Benson, Merrill D.; Tennent, Glenys A.; Pepys, Mark B.; Fraser, Paul E. (Neurobiology Division, Med. Res. Council Cent., Lab. Mol. Biol., Cambridge, CB2 2QH, UK). Journal of Molecular Biology, 300(5), 1033-1039 (English) 2000. CODEN: JMOBAK. ISSN: 0022-2836. Publisher: Academic Press.

AB Tissue deposition of normally **sol.** proteins, or their fragments, as insol. amyloid fibrils causes the usually fatal, acquired and hereditary systemic amyloidoses and is assocd. with the pathol. of Alzheimer's disease, type 2 diabetes and the transmissible spongiform encephalopathies. Although each type of amyloidosis is characterized by a specific amyloid fibril protein, the deposits share pathognomonic histochem. properties and the structural morphol. of all amyloid fibrils is very similar. We have previously demonstrated that transthyretin amyloid fibrils contain four constituent protofilaments packed in a square array. Here, we have used cross-correlation techniques to av. electron microscopy images of multiple cross-sections in order to reconstruct the sub-structure of ex vivo amyloid fibrils composed of amyloid A protein, monoclonal Ig .lambda. light chain, Leu60Arg variant apolipoprotein AI, and Asp67His variant lysozyme, as well as synthetic fibrils derived from a ten-residue **peptide** corresponding to the A-strand of transthyretin. All the fibrils had an electron-lucent core but the packing arrangement comprised five or six protofilaments rather than four. The structural similarity that defines amyloid fibers thus exists principally at the level of .beta.-sheet folding of the polypeptides within the protofilament, while the different types vary in the supramol. assembly of their protofilaments. (c) 2000 Academic Press.

L6 ANSWER 16 OF 49 MEDLINE DUPLICATE 1

2001040337 Document Number: 21000419. PubMed ID: 11070162. Inhibition of amyloid fiber assembly by both BiP and its target **peptide**. Davis P D; Raffen R; Dul L J; Vogen M S; Williamson K E; Stevens J F; Argon Y. (Department of Pathology and Committee on Immunology, The University of Chicago, Illinois 60637, USA.) IMMUNITY, (2000 Oct) 13 (4) 433-42. Journal code: 9432918. ISSN: 1074-7613. Pub. country: United States. Language: English.

AB **Immunoglobulin light chain** (LC) normally is a **soluble**, secreted protein, but some LC assemble into ordered fibrils whose deposition in tissues results in amyloidosis and organ failure. Here we reconstitute fibril formation in vitro and show that

preformed fibrils can nucleate polymerization of **soluble** LC. This prion-like behavior has important physiological implications, since somatic mutations generate multiple related LC sequences. Furthermore, we demonstrate that fibril formation in vitro and aggregation of whole LC within cells are inhibited by BiP and by a synthetic **peptide** that is identical to a major LC binding site for BiP. We propose that LC form fibrils via an interprotein loop swap and that the underlying conformational change should be amenable to drug therapy.

L6 ANSWER 17 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

2001153538 EMBASE Cloning and expression in Pichia pastoris of a genetically engineered single chain antibody against the rat transferrin receptor. Boado R.J.; Ji A.; Pardridge W.M.. Dr. R.J. Boado, Department of Medicine, UCLA School of Medicine, Los Angeles, CA 90095-1682, United States. rboado@mednet.ucla.edu. Journal of Drug Targeting 8/6 (403-412) 2000. Refs: 24.
ISSN: 1061-186X. CODEN: JDTAEH. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB The present investigation describes the construction of a genetically engineered single chain antibody (scFv) against the rat transferrin receptor (OX26), and demonstrates that this scFv antibody can be fully processed and expressed as a **soluble** secreted molecule in the methylotrophic yeast Pichia pastoris. Restriction endonuclease sites located at both 5'- and 3'-flanking regions of OX26 coding region in the prokaryote pOPE-OX26 vector were engineered to incorporate yeast compatible restriction endonuclease sites (i.e. EcoRI and SmaI or AvrII). The modified OX26 cDNA was subcloned into the Pichia expression vectors pPIC9 and pHIL-S1. An OX26 scFv high producer clone [GS115 His(+) Mut(+) (pPIC-OX26 SacI)] was isolated and used for large-scale production and characterization. Because the engineered scFv contains both a c-myc tag and a (His)(5) tail, the OX26 scFv was purified to homogeneity by immobilized metal affinity chromatography. The identity of the OX26 scFv was confirmed by Western blot analyses with both anti c-myc and anti poly-His antibodies. Minor immuno-reactive bands corresponding to hyperglycosylated and partially processed .alpha.-factor leader prosequence were also detected in the purified OX26 scFv, and these contaminants were markedly reduced when the expression of the OX26 scFv was performed in minimal methanol medium buffered with phosphate at pH = 7. The present investigation suggests that this expression system may be useful for the production of anti-receptor single chain antibodies that can be used as brain drug delivery vectors.

L6 ANSWER 18 OF 49 MEDLINE

2000418704 Document Number: 20395355. PubMed ID: 10941907. Single-chain antibodies against human insulin-like growth factor I receptor: expression, purification, and effect on tumor growth. Li S L; Liang S J; Guo N; Wu A M; Fujita-Yamaguchi Y. (Department of Molecular Biology, Beckman Research Institute of the City of Hope, Duarte, CA 91010, USA.) CANCER IMMUNOLOGY, IMMUNOTHERAPY, (2000 Jul) 49 (4-5) 243-52. Journal code: 8605732. ISSN: 0340-7004. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Insulin-like growth factors (IGF) I and II are potent mitogens for a variety of cancer cells. The proliferative and anti-apoptotic actions of IGF are mediated by the IGF-I receptor (IGF-IR), to which both IGF-I and IGF-II bind with high affinity. To investigate the mitogenic and anti-apoptotic activities of IGF-IR and to achieve better inhibition of IGF-IR function, single-chain antibodies against human IGF-IR (alphaIGF-IR scFvs) were constructed and expressed. IgG cDNA encoding variable regions of light and heavy chains (VL and VH) from mouse IgG were cloned from a hybridoma producing the 1H7 alphaIGF-IR monoclonal antibody [Li et al., Biochem Biophys Res Commun 196: 92-98 (1993)]. The splice-overlap extension polymerase chain reaction was used to assemble a gene encoding the alphaIGF-IR scFv, including the N-terminal signal **peptide**,

VL, linker **peptide**, VH, and C-terminal DYKD tag. Two types of **soluble** alphaIGF-IR scFvs, a prototype alphaIGF-IR scFv and its alternative type alphaIGF-IR scFv-Fc, were constructed and expressed in murine myeloma cells. alphaIGF-IR scFv-Fc, containing the human IgG1 Fc domain, was stably expressed in NS0 myeloma cells, using a glutamine synthase selection system, and purified from the conditioned medium of stable clones by protein-A--agarose chromatography. Levels of alphaIGF-IR scFv-Fc expression ranged from 40 mg/l to 100 mg/l conditioned medium. Sodium dodecyl sulfate/polyacrylamide gel electrophoresis analysis under reducing and nonreducing conditions indicated that alphaIGF-IR scFv-Fc is a dimeric antibody. alphaIGF-IR scFv-Fc retained general characteristics of the parental 1H7 monoclonal antibody except that its binding affinity for IGF-IR was estimated to be approximately 10(8) M(-1), which was one-order of magnitude lower than that of 1H7 monoclonal antibody. Injection of alphaIGF-IR scFv-Fc (500 microg/mouse, twice a week) significantly suppressed MCF-7 tumor growth in athymic mice. These results suggest that the alphaIGF-IR scFv-Fc is a first-generation recombinant alphaIGF-IR for the potential development of future alphaIGF-IR therapeutics.

L6 ANSWER 19 OF 49 MEDLINE DUPLICATE 2

2000105212 Document Number: 20105212. PubMed ID: 10637303. Dissociation from BiP and retrotranslocation of unassembled **immunoglobulin light chains** are tightly coupled to proteasome activity.
Chillaron J; Haas I G. (Biochemie-Zentrum Heidelberg, D-69120 Heidelberg, Germany.) MOLECULAR BIOLOGY OF THE CELL, (2000 Jan) 11 (1) 217-26.
Journal code: 9201390. ISSN: 1059-1524. Pub. country: United States.
Language: English.

AB Unassembled **immunoglobulin light chains** expressed by the mouse plasmacytoma cell line NS1 (kappa(NS1)) are degraded in vivo with a half-life of 50-60 min in a way that closely resembles endoplasmic reticulum (ER)-associated degradation (). Here we show that the **peptide** aldehydes MG132 and PS1 and the specific proteasome inhibitor lactacystin effectively increased the half-life of kappa(NS1), arguing for a proteasome-mediated degradation pathway. Subcellular fractionation and protease protection assays have indicated an ER localization of kappa(NS1) upon proteasome inhibition. This was independently confirmed by the analysis of the folding state of kappa(NS1) and size fractionation experiments showing that the **immunoglobulin light chain** remained bound to the ER chaperone BiP when the activity of the proteasome was blocked. Moreover, kinetic studies performed in lactacystin-treated cells revealed a time-dependent increase in the physical stability of the BiP-kappa(NS1) complex, suggesting that additional proteins are present in the older complex. Together, our data support a model for ER-associated degradation in which both the release of a **soluble** nonglycosylated protein from BiP and its retrotranslocation out of the ER are tightly coupled with proteasome activity.

L6 ANSWER 20 OF 49 CAPLUS COPYRIGHT 2002 ACS

1999:344861 Document No. 131:4240 Immunoglobulin molecules having a synthetic variable region and modified specificity. Burch, Ronald M. (Euro-Celtique, S.A., Bermuda). PCT Int. Appl. WO 9925378 A1 19990527, 123 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US24302 19981113. PRIORITY: US 1997-65716 19971114; US 1998-81403 19980410.

AB The invention provides modified Ig mols., particularly antibodies, that

immunospecifically bind a first member of a binding pair which binding pair consists of the first member and a second member, which Igs have a variable domain contg. one or more complimentary detg. regions that contain the amino acid sequence of a binding site for the second member of the binding pair. The first member is a tumor antigen or an antigen of an infectious disease agent, and the second member is a mol. on the surface of an immune cell. The invention further provides for therapeutic and diagnostic use of the modified Ig.

L6 ANSWER 21 OF 49 CAPLUS COPYRIGHT 2002 ACS

1999:297317 Document No. 130:295539 Construction of chimeric **soluble** MHC complexes. Rhode, Peter R.; Acevedo, Jorge; Burkhardt, Martin; Jiao, Jin-an; Wong, Hing C. (Sunol Molecular Corporation, USA). PCT Int. Appl. WO 9921572 A1 19990506, 148 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US21520 19981013. PRIORITY: US 1997-960190 19971029.

AB The authors disclose the construction and expression of **sol**. single-chain (s.c.) MHC class II mols. In one aspect, the s.c.-MHC class II mols. include a .beta.2 chain modification, e.g., deletion of essentially the entire class II .beta.2 domain. In another aspect, the invention features single-chain MHC class II which contain an **Ig light chain** const. region fragment (CL). The CL fragment allows multimerization of single-chain monomers of identical or disparate MHC specificity or formation of heteromeric mols. with effector function (e.g., single-chain antibodies). In addn., the **sol**. MHC class II mols. can be constructed for exogenous loading of cognate **peptides** or the requisite **peptides** can be included in the single-chain constructs themselves. In one example, single-chain I-Ad mols. were constructed as fusion proteins with T-cell epitopes from either ovalbumin or glycoprotein D of herpes simplex virus. These constructs were shown to stimulate interleukin-2 prodn. by their resp. antigen-specific T-cells. MHC complexes of the invention are useful for a variety of applications including: (1) in vitro screens for identification and isolation of **peptides** that modulate activity of selected T-cells, including **peptides** that are T cell receptor antagonists and partial agonists, and (2) methods for suppressing or inducing an immune response in a mammal.

L6 ANSWER 22 OF 49 CAPLUS COPYRIGHT 2002 ACS

1999:244685 Document No. 130:266368 **Soluble** single-chain T-cell receptor proteins. Weidanz, Jon A.; Card, Kimberlyn F.; Wong, Hing C. (Sunol Molecular Corporation, USA). PCT Int. Appl. WO 9918129 A1 19990415, 145 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US20263 19980928. PRIORITY: US 1997-943086 19971002.

AB The authors disclose the prepn. and characterization of fully **sol**. and functional single-chain T-cell receptor proteins. The **sol**. TCR receptor fusion proteins contain an **Ig light chain** const. region (or fragment thereof) covalently linked to a single-chain TCR comprised of a V-.alpha. chain covalently linked to a V-.beta. chain by a **peptide** linker sequence. In one example,

sol. single-chain TCR receptors, recognizing a determinant of ovalbumin, suppressed the antigen-specific proliferative response of T-cells. The single-chain T-cell receptor proteins have a variety of uses including basic research, diagnostic, and therapeutic application.

L6 ANSWER 23 OF 49 CAPLUS COPYRIGHT 2002 ACS
1999:113797 Document No. 130:166800 **Soluble** fusion proteins of aggregate-forming proteins and the study of diseases associated with protein aggregate formation. Wanker, Erich; Lehrach, Hans; Scherzinger, Eberhard; Bates, Gillian (Max-Planck-Gesellschaft zur Forderung der Wissenschaften e.V., Germany). PCT Int. Appl. WO 9906545 A2 19990211, 62 pp. DESIGNATED STATES: W: CA, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-EP4811 19980731.
AB Fusion proteins of aggregate-forming proteins and solubilizing **peptides** are described for use in elucidating the mechanism, onset or progress of diseases assocd. with the formation of amyloid-like fibrils or protein aggregates. The method is for use in the study of neurol. diseases such as Huntington's and Alzheimer's. The fusion proteins can also be used to screen for inhibitors of aggregation that may be of therapeutic use. Genes for a series of fusion proteins polyglutamine repeat expansion variants (20, 30, or 51 glutamine repeats) of huntingtin and glutathione-S-transferase were constructed by std. methods and manufd. in Escherichia coli using a hexahistidine for affinity purifn. The fusion proteins were **sol**. but cleavage of the 51 glutamine repeat variant (HD51) with trypsin led to the formation of insol. aggregates of the huntingtin. HD51 aggregated in vitro to form amyloid-like birefringent fibrils after liberation by trypsin cleavage, but the shorter repeat variants HD20 and HD30 did not do so. Similar effects were seen in vivo in COS-1 cells.

L6 ANSWER 24 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
1999220368 EMBASE Monoclonal autoantibodies from patients with autoimmune diseases: Synovial fluid B lymphocytes of a patient with rheumatoid arthritis produced an IgG.lambda. antibody recognizing J-sequences of Ig.kappa. chains in a conformation-dependent way. Von Landenberg P.; Rzepka R.; Melchers I.. Dr. I. Melchers, Klin. Forschergruppe Rheumatologie, Klinikum, Albert-Ludwigs-Universitat, Breischer Str. 64, D-79106 Freiburg, Germany. Melchers@nz11.ukl.uni-freiburg.de.
Immunobiology 200/2 (205-214) 1999.
Refs: 41.
ISSN: 0171-2985. CODEN: ZIMMDO. Pub. Country: Germany. Language: English. Summary Language: English.
AB Synovial fluid B cells from a patient with seronegative rheumatoid arthritis were immortalized by electrofusion. The specificity of clone FKN-E12 (IgG1.lambda.) was analysed by screening a phage display random **peptide** library. One heptamer sequence was identified (RASFp1 = HLTFGPG). Three human IgG.kappa. antibodies contained a highly homologous sequence (xLTFGPG) at the junction of V- and J-regions. Homologies were also found in distinct humans (J.kappa.3, J.kappa.4) and murine (J.kappa.5) J.kappa.-sequences (TFGPG, LTFGxG), and to a lower degreee in all remaining J.kappa.-sequences (TFGxG). Binding and binding inhibition assays showed that FKN-E12 bound to .kappa. light chains tested in a conformation-dependent way: it reacted only with IgG.kappa. or IgA.kappa. chains adhered to a plastic surface, but not in **soluble** form. In conclusion, FKN-E12 detects a conformational epitope on probably all .kappa. light chains, which could be definded by screening a phage library displaying linear epitopes.

L6 ANSWER 25 OF 49 MEDLINE
2000075200 Document Number: 20075200. PubMed ID: 10607222. Human recombinant single-chain antibody fragments, specific for the hypervariable region 1 of hepatitis C virus, from immune phage-display

libraries. Zhai W; Davies J; Shang D Z; Chan S W; Allain J P. (Division of Transfusion Medicine, Department of Haematology, University of Cambridge, UK.) JOURNAL OF VIRAL HEPATITIS, (1999 Mar) 6 (2) 115-24. Journal code: 9435672. ISSN: 1352-0504. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The hypervariable region 1 (HVR1) of hepatitis C virus (HCV) may contain a potential neutralization site and the generation of human single-chain antibody fragments (scFv) to HVR1 may therefore provide a useful tool for the study of HCV. In this report, we have isolated and characterized three anti-HVR1 scFv clones from two patient-derived phage-displayed libraries and HCV HVR1 **peptides**. scFv S52/20 and S53/6 were selected with serologically cross-reactive HVR1 **peptides**. scFv p3f10 was obtained by screening the library from patient MH with an autologous HVR1 **peptide**. Nucleotide sequencing showed that the VH chains and Vkappa chains of all three scFv antibodies were derived from VH3 and Vkappa1 family germline V-genes, respectively. The specificity and affinity of the recombinant scFv antibodies were examined by enzyme-linked immunosorbent assay (ELISA) and an affinity biosensor, using HVR1 **peptides**. S52/20 scFv binding to S52 HVR1 **peptide** was blocked by preincubation with **soluble peptide** S52 and was partially competed by one of three HCV-infected patient sera. In addition, scFv S52/20 blocked the binding of HCV-susceptible Molt-4 cells to immobilized S52 **peptide**. This study demonstrates that recombinant human scFv antibodies to HCV HVR1 can be produced in vitro and directly confirms that HVR1 of HCV elicits highly specific antibodies. The very high specificity of these antibodies to HVR1 may limit their potential use in passive immunization therapy against HCV, and further engineering of the scFvs needs to be performed to generate broad-spectrum blocking scFvs.

L6 ANSWER 26 OF 49 MEDLINE

1999261573 Document Number: 99261573. PubMed ID: 10331188. Human single-chain Fv fragments from a combinatorial library using the loxP-Cre recombination system. Biard-Piechaczyk M; Teulon I; Peraldi-Roux S; Del Rio M; Pau B; Embleton J. (CNRS UMR 9921, UFR Sciences Pharmaceutiques et Biologiques, Montpellier, France.. martinep@pharma.univ-montpl.fr) . HUMAN ANTIBODIES, (1999) 9 (1) 67-77. Journal code: 9711270. ISSN: 1093-2607. Pub. country: Netherlands. Language: English.

AB A human scFv display library has been constructed from peripheral blood lymphocytes of a patient suffering from Hashimoto's thyroiditis. Upon induction of Cre recombinase, the amplified VH and VL genes were recombined via two loxP sites inserted in amplification primers to construct in vitro scFv genes. Either **soluble** scFvs or scFvs displayed on phage were screened for binding to human thyroglobulin after two pannings with this antigen. Three scFvs were obtained which showed very similar nucleotidic sequences. The VH genes expressed display 96.4% nucleotide sequence homology with the germline VH251 gene, one of the two functional members of the small VH5 family and are mutated in sites already described as "selectively neutral" mutations and the VL genes are close to the germline DPL8 gene. These scFvs bind not only to human thyroglobulin but also to other self and exogenous antigens.

L6 ANSWER 27 OF 49 CAPLUS COPYRIGHT 2002 ACS

1998:323257 Document No. 129:1412 Developing **soluble** analogs of insoluble proteins retaining biological activities by systematic deletion of codons from the gene. Prusiner, Stanley B.; Cohen, Fred E.; Muramoto, Tamaki (Regents of the University of California, USA). PCT Int. Appl. WO 9820022 A1 19980514, 41 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC,

ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US6227 19970415. PRIORITY: US 1996-740947 19961105.

AB A method of developing **sol**. deletion analogs of an insol. protein that mimic the characteristics of an insol. native protein. These proteins are shorter than their parent sequences, are more **sol**. than the original protein and retain basic biol. characteristics such as not being subject to enzymic digestion and causing disease. These proteins are obtained by systematically removing codons from the gene and expressing the truncated gene to manuf. the protein for characterization. These **sol**. analogs. can be used to study processes in which the insol. form plays a role, in the prepn. of antibodies to the protein, and in the development of analogs that can be used to control protein interactions involved in disease processes. The systematic generation of deletion analogs of prion proteins based upon studies of the soln. interaction of **peptides** of the protein is described.

L6 ANSWER 28 OF 49 CAPLUS COPYRIGHT 2002 ACS

1998:176019 Document No. 128:242896 Humanized immunoglobulin reacting specifically with Fas ligand or active fragments thereof and region inducing apoptosis originating in Fas ligand. Okumura, Ko; Nakata, Motomi; Higuchi, Hirofumi; Ushio, Yoshitaka; Maeda, Hiroaki; Eda, Yasuyuki (Sumitomo Electric Industries, Ltd., Japan; Okumura, Ko; Nakata, Motomi; Higuchi, Hirofumi; Ushio, Yoshitaka; Maeda, Hiroaki; Eda, Yasuyuki). PCT Int. Appl. WO 9810070 A1 19980312, 358 pp. DESIGNATED STATES: W: AU, CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1997-JP2983 19970827. PRIORITY: JP 1996-231742 19960902; JP 1996-271546 19960920.

AB A novel humanized Ig reacting specifically with a Fas ligand and active fragments thereof are provided and a region on a Fas ligand which is important in inhibiting apoptosis induced by cells with Fas expression on the basis of the Fas-Fas ligand interaction is clarified. The novel humanized Ig and active fragments thereof are prepd. by the recombinant DNA techniques from hybridomas which produce a monoclonal antibody reacting specifically with a Fas ligand. This Ig can inhibit physiol. reactions between a Fas ligand and Fas, typified by apoptosis. By specifying the region participating in the induction of apoptosis on a Fas ligand, there have been constructed recombinant proteins and **peptides** which react specially with the amino acids contained in this region to thereby inhibit apoptosis and are thus applicable to novel remedies, clin. diagnostic drugs, etc. The humanized Ig and Fas ligand epitope fragments are useful diagnosis and therapy of AIDS, bone marrow transplant rejection or graft vs. host disease, acute hepatitis, autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis and diabetes.

L6 ANSWER 29 OF 49 MEDLINE DUPLICATE 3

1998049562 Document Number: 98049562. PubMed ID: 9388240. Systematic exploration of the antigen binding activity of synthetic **peptides** isolated from the variable regions of immunoglobulins. Laune D; Molina F; Ferrieres G; Mani J C; Cohen P; Simon D; Bernardi T; Piechaczyk M; Pau B; Granier C. (CNRS UMR 9921. Faculte de Pharmacie, Avenue Charles Flahault, 34000 Montpellier, France.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Dec 5) 272 (49) 30937-44. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Sets of short (12 residues) cellulose-bound synthetic overlapping **peptides** derived from the sequences of the variable regions of the heavy and light chains of three different antibodies (an anti-thyroglobulin antibody, the HyHEL-5 anti-lysozyme antibody, and an anti-angiotensin II antibody) were used to systematically assess the antigen binding capacity of **peptides** from the antibody paratope outside their natural molecular context. **Peptides** enclosing one or several of the complementarity determining region (CDR) residues had antigen binding activity, although the most active **peptides** were

not necessarily those bearing the greatest number of CDR residues. Several residues from the framework region, preceding or following the CDR, were found to play a role in binding. Affinity constants from 4.1 x 10(-7) to 6.7 x 10(-8) M-1 for the **soluble** form of 9 lysozyme-binding dodecapeptides were measured by BIAcore analysis. Alanine scanning of lysozyme-binding hexapeptides from the HyHEL-5 sequence identified 38 residues important for binding, of which 22 corresponded to residues that had been shown by x-ray crystallography to be at the interface between HyHEL-5 and lysozyme. Our results could be of interest for the rational identification of biologically active **peptides** derived from antibody sequences and in providing an experimental basis for mutagenesis of the antibody paratope.

L6 ANSWER 30 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

97255275 EMBASE Document No.: 1997255275. Production and characterization of a recombinant anti-MUC1 scFv reactive with human carcinomas. Denton G.; Sekowski M.; Spencer D.I.R.; Hughes O.D.M.; Murray A.; Denley H.; Tendler S.J.B.; Price M.R.. G. Denton, Cancer Research Laboratories, Department of Pharmaceutical Science, University of Nottingham, University Park, Nottingham NG7 2RD, United Kingdom. British Journal of Cancer 76/5 (614-621) 1997.
Refs: 28.
ISSN: 0007-0920. CODEN: BJCAAI. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Recombinant single-chain fragments (scFv) of the murine anti-MUC1 monoclonal antibody C595 have been produced using the original hybridoma cells as a source of variable heavy (V(H))- and variable light (V(L))-chain-encoding antibody genes. The use of the polymerase chain reaction (PCR), bacteriophage (phage) display technology and gene expression systems in E. coli has led to the production of **soluble** C595 scFv. The scFv has been purified from the bacterial supernatant by **peptide** epitope affinity chromatography, leading to the recovery of immunoreactive C595 scFv, which was similar in activity to the C595 parent antibody. Analysis by DNA sequencing, SDS-PAGE and Western blotting has demonstrated the integrity of the scFv, while ELISA, FACScan analysis, fluorescence quenching, quantitative immunoreactivity experiments and immunohistochemistry confirm that the activity of the scFv compares favourably with that of the parent antibody. The retention of binding activity to MUC1 antigen on human bladder and breast carcinoma tissue specimens illustrates the potential application of this novel product as an immunodiagnostic and immunotherapeutic reagent.

L6 ANSWER 31 OF 49 CAPLUS COPYRIGHT 2002 ACS

1997:16729 Document No. 126:130370 Molecular cloning, expression, and characterization of a functional single-chain Fv antibody to the mycotoxin zearalenone. Yuan, Qiaoping; Clarke, James R.; Zhou, Hui-Ren; Linz, John E.; Pestka, James J.; Hart, L. Patrick (Departments of Botany and Plant Pathology, Michigan State University, East Lansing, MI, 48824, USA). Appl. Environ. Microbiol., 63(1), 263-269 (English) 1997. CODEN: AEMIDF. ISSN: 0099-2240. Publisher: American Society for Microbiology.

AB The heavy-chain and kappa light-chain variable region genes of an antizearalenone hybridoma cell line (2G3-6E3-2E2) were isolated by PCR and joined by a DNA linker encoding **peptide** (Gly4Ser)3 as a single-chain Fv (scFv) DNA fragment. The scFv DNA fragment was cloned into a phagemid (pCANTAB5E) and expressed as a fusion protein with E tag and phage M13 p3 in Escherichia coli TG1. In the presence of helper phage M13K07, the scFv fusion protein was displayed on the surfaces of recombinant phages. High-affinity scFv phages were enriched through affinity selection in microtiter wells coated with zearalenone-ovalbumin conjugate. The selected recombinant phages were used to infect E. coli HB2151 for the prodn. of **sol**. scFv antibodies. One selected clone (pQY1.5) in HB2151 secreted a **sol**. scFv antibody (QY1.5) with a high zearalenone-binding affinity (concn. required for 50%

inhibition of binding, 14 ng/mL), similar to that of parent monoclonal antibody in a competitive indirect ELISA. However, scFv QY1.5 exhibited higher cross-reactivity with zearalenone analogs and had greater sensitivity to methanol destabilization than the parent monoclonal antibody did. Nucleotide sequence analyses revealed that the light-chain portion of scFv OY1.5 had a nucleotide sequence identity of 97% to a mouse germ line gene VK23.32 in mouse kappa light-chain variable region subgroup V, whereas the heavy-chain nucleotide sequence was classified as mouse heavy-chain subgroup III (D) but without any closely related members having highly homologous complementarity-detg. region sequences. The potential of **sol**. scFv QY1.5 for routine screening of zearalenone and its analogs was demonstrated with zearalenone-spiked corn exts.

L6 ANSWER 32 OF 49 CAPLUS COPYRIGHT 2002 ACS

1997:574175 Document No. 127:276898 Sequence analysis and bacterial production of the anti-c-myc antibody 9E10: the VH domain has an extended CDR-H3 and exhibits unusual solubility. Schiweck, Wolfram; Buxbaum, Britta; Schaetzlein, Christian; Neiss, Hans Guenther; Skerra, Arne (Institut fuer Biochemie, Technische Hochschule, Petersenstr. 22, Darmstadt, D-64287, Germany). FEBS Letters, 414(1), 33-38 (English) 1997. CODEN: FEBLAL. ISSN: 0014-5793. Publisher: Elsevier.

AB The cDNAs for the two variable domains of the antibody 9E10 were cloned from the hybridoma cell line. A chimeric 9E10 Fab fragment was produced in E. coli under control of the tightly controlled tetracycline promoter. The functional Fab fragment was isolated in a single step via a His6-tag, which also served for its recognition by a nickel chelate-alk. phosphatase conjugate. Thus, the recombinant Fab fragment permitted the immunochem. detection of the myc tag in a sandwich ELISA. The dissocn. const. for the interaction with the myc tag **peptide** was detd. as 80 nM by fluorescence titrn. To produce the smaller 9E10 Fv fragment it was found that its VH domain alone can be readily isolated from E. coli as a **sol**. protein. This unusual behavior may be explained by the 18 amino acid-long CDR-H3 and could be of value in the design of 'single domain' antibodies.

L6 ANSWER 33 OF 49 CAPLUS COPYRIGHT 2002 ACS

1997:448808 Document No. 127:160316 Expression of the variable region genes of the monoclonal antibodies against metal-bound tetrapeptide in Escherichia coli. Han, Liying; Shen, Liying; Chen, Changqing; Su, Chengzhi (Fourth Military Med. Univ., Xi'an, 710032, Peop. Rep. China). Shengwu Huaxue Yu Shengwu Wuli Xuebao, 28(6), 583-589 (Chinese) 1996. CODEN: SHWPAU. ISSN: 0582-9879. Publisher: Shanghai Kexue Jishu Chubanshe.

AB The variable region genes of the light and heavy chains obtained from 3 stems of McAb against metal-bound tetrapeptides were joined into a single chain by a linker. A 39 bp fragment of the N-terminal of Calcitonin gene-related **peptide** (CGRP) was joined to the C-terminal of the heavy chain to constitute the Lv-liner-Hv-CGRP single chain gene which was cloned into the vector pTC01 and expressed in E.coli 71/18. The mol. wt. of the expressed product was approx. 26 KD as shown by SDS-PAGE. Its expression level was 20-30% of the total cellular proteins. The product was a **sol**. protein and showed binding activity with its hapten by indirect ELISA assay.

L6 ANSWER 34 OF 49 MEDLINE DUPLICATE 4

96348999 Document Number: 96348999. PubMed ID: 8738212. Production and characterization of anti-human interferon gamma receptor antibody fragments that inhibit cytokine binding to the receptor. Bridges A; Stuart F; Spath J; Lang S; Henke C; Birch A; Robinson J A. (Institute of Organic Chemistry, University of Zurich, Switzerland.) PROTEIN ENGINEERING, (1996 Apr) 9 (4) 365-70. Journal code: 8801484. ISSN: 0269-2139. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Three single-chain antibody fragments that recognize the extracellular human interferon gamma receptor alpha-chain (IFN gamma R), and inhibit the binding of human IFN gamma, have been produced in Escherichia coli. These fragments are derived from murine anti-receptor monoclonal antibodies, and comprise the variable heavy (VH) domain linked to the variable light (VL) chain through a 15 amino acid linker [(GGGGS)3]. Using surface plasmon resonance technology (BIAcore), the **soluble** proteins were shown to retain a high affinity for recombinant IFN gamma R, and by radioimmunoassay to possess a high inhibitory activity towards IFN gamma-binding to human Raji cells. The antibody fragments most likely recognize epitopes that overlap the cytokine binding site on the receptor surface. Attempts to dissect further the antibodies to isolated VH- and VL-chains and to synthetic linear and cyclic **peptides** derived from the individual complementarity determining regions failed to afford fragments with significant IFN gamma R binding affinity. Nevertheless, these native-like variable region fragments and petidomimetics derived from them are of interest in the design of novel IFN gamma R antagonists.

L6 ANSWER 35 OF 49 MEDLINE DUPLICATE 5

96375171 Document Number: 96375171. PubMed ID: 8781541. Efficient vasoactive intestinal polypeptide hydrolyzing autoantibody light chains selected by phage display. Tyutyulkova S; Gao Q S; Thompson A; Rennard S; Paul S. (Department of Anesthesiology, University of Nebraska Medical Center, Omaha, USA.) BIOCHIMICA ET BIOPHYSICA ACTA, (1996 Aug 23) 1316 (3) 217-23. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB An **immunoglobulin light chain** (L chain) library derived from the peripheral blood lymphocytes of a patient with asthma was cloned into a phagemid vector. Phage particles displaying L chains capable of binding vasoactive intestinal polypeptide (VIP) were isolated by affinity chromatography. Two VIP binding L chains were expressed in Escherichia coli in **soluble** form and purified to electrophoretic homogeneity by metal chelating and protein L affinity chromatography. Both L chains catalyzed the hydrolysis of [tyr10-125I]VIP substrate. The catalytic activity eluted at the molecular mass of the monomer form of the L chain (28 kDa) from a gel filtration column. The activity was bound by immobilized anti-kappa-chain antibody. A control recombinant L chain displayed no catalytic activity. Hydrolysis of VIP by the catalytic L chains was saturable and consistent with Michaelis-Menten kinetics. The turnover of the L chains was moderate (0.22 and 2.21/min) and their Km values indicated comparatively high affinity recognition of VIP[111 and 202 nM), producing catalytic efficiencies comparable to or greater than trypsin. Unlike trypsin, the L chains did not display detectable cleavage of casein, suggesting a catalytic activity specialized for VIP. Comparisons of the nucleotide sequences of the L chain cDNA with their putative germ-line counterparts suggested the presence of several replacement mutations in the complementarity determining regions (CDRs). These observations suggest: (a) Retention or acquisition of catalytic activity by the L chains is compatible with affinity maturation of antibodies; and (b) The autoimmune L chain repertoire can serve as a source of substrate-specific and efficient catalysts.

L6 ANSWER 36 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

95116769 EMBASE Document No.: 1995116769. A high affinity digoxin-binding protein displayed on M13 is functionally identical to the native protein. Tang P.M.; Foltz L.A.; Mahoney W.C.; Schueler P.A.. Molecular Diagnostics, R and D, Boehringer Mannheim Corp., 9115 Hague Rd.,Indianapolis, IN 46250, United States. Journal of Biological Chemistry 270/14 (7829-7835) 1995. ISSN: 0021-9258. CODEN: JBCHA3. Pub. Country: United States. Language: English. Summary Language: English.

AB Phage display of **peptides** and proteins has successfully been employed to produce binding molecules of altered affinity. Little is known, however, regarding the impact on affinity measurements of

phage-displayed molecules compared to their native freely **soluble** configuration. That identical affinities can be obtained was shown by Scatchard analysis of the native antibody, its single chain derivative (scFv), and its phage-displayed single chain counterpart for the ligand digoxin. No significant difference, within one standard deviation, was detected in affinity for digoxin when the phage- displayed scFv was compared to either its **soluble** scFv form or the purified antibody. In addition, no change in binding specificity was detected, within two standard deviations, when the binding proteins were challenged with two commonly cross-reactive compounds (dihydrodigoxin and digitoxin). That phage- display can be employed for molecules having high binding affinities (K(d) of 6 x 10-11 M) is also shown.

L6 ANSWER 37 OF 49 MEDLINE

95332275 Document Number: 95332275. PubMed ID: 7608138. Specific binding of a synthetic **peptide** derived from an antibody complementarity determining region to phosphatidylserine. Igarashi K; Asai K; Kaneda M; Umeda M; Inoue K. (Department of Health Chemistry, Faculty of Pharmaceutical Sciences, University of Tokyo.) JOURNAL OF BIOCHEMISTRY, (1995 Feb) 117 (2) 452-7. Journal code: 0376600. ISSN: 0021-924X. Pub. country: Japan. Language: English.

AB We have established a series of monoclonal antibodies that bind to phosphatidylserine (PS). One mAb, PS4A7, showed a strict specificity for PS and distinguished the stereospecific configuration of its serine moiety. We determined the amino acid sequences of the heavy and light chain variable regions of PS4A7, and examined the reactivity of the synthetic **peptides** corresponding to the complementarity determining region (CDR) of the mAb with phospholipids. We found that a 12-amino acid synthetic **peptide** corresponding to the third CDR of the heavy chain (amino acid residues 93-102, referred to as CDR3-H) bound specifically to PS. Although the affinity of the **peptide** to PS was markedly lower, the **peptide** was shown to bind to 1,2-diacyl-sn-glycero-3-phospho-L-serine (PS), but not to 1,2-diacyl-sn-glycero-3-phospho-D-serine, showing a similar specificity to that of PS4A7. The specific binding of the CDR3-H **peptide** to PS was confirmed by ELISA and TLC-immunostaining assay. The interaction between the CDR3-H **peptide** and water-**soluble** PS-derivatives was investigated by inhibition of the ELISA. PS effectively inhibited the binding and phosphoserine showed a weak but significant inhibition, but no appreciable inhibition was observed with serine. These observations suggest that the CDR3-H **peptide** plays a major role in the interaction of PS4A7 with the phosphoserine residue of the PS molecule.

L6 ANSWER 38 OF 49 MEDLINE DUPLICATE 6

95031003 Document Number: 95031003. PubMed ID: 7944337. Selection of functional human **immunoglobulin light chains** from a phage-display library. Tyutyulkova S; Paul S. (Department of Anesthesiology, University of Nebraska Medical Center, Omaha.) APPLIED BIOCHEMISTRY AND BIOTECHNOLOGY, (1994 May-Jun) 47 (2-3) 191-7; discussion 198. Journal code: 8208561. ISSN: 0273-2289. Pub. country: United States. Language: English.

AB Human kappa-light chains (L chains) were amplified by the reverse transcriptase-polymerase chain reaction (PCR) and cloned into a phagemid vector. Phage particles displaying L chains were fractionated on immobilized vasoactive intestinal **peptide** (VIP). The resultant phage preparation displayed saturable binding of (tyr10-125I)VIP. One of the L-chain clones (hk13) was deduced to be related to subgroup I of kappa-light chains based on its nucleotide sequence. The VIP binding activity of the **soluble** and phage-displayed form of this L chain was confirmed by radioimmunoassay and ELISA, respectively. These observations demonstrate the potential of selecting antigen-specific L chains from phage-display libraries.

L6 ANSWER 39 OF 49 MEDLINE DUPLICATE 7
94355703 Document Number: 94355703. PubMed ID: 8075437. Characterization of the amyloid fibril from primary localized cutaneous nodular amyloidosis associated with Sjogren's syndrome. Inazumi T; Hakuno M; Yamada H; Tanaka M; Naka W; Tajima S; Harada T; Nishikawa T. (Department of Dermatology, Urawa Municipal Hospital, Japan.) DERMATOLOGY, (1994) 189 (2) 125-8. Ref: 15. Journal code: 9203244. ISSN: 1018-8665. Pub. country: Switzerland. Language: English.

AB BACKGROUND: Primary localized cutaneous nodular amyloidosis (PLCNA) is a rare disease, and its pathogenesis of amyloid deposition is still unknown. OBJECTIVE: The purpose of this study was to know the origin of amyloid in PLCNA. METHODS: Water-**soluble** amyloid fibrils were isolated from the skin and resolved on SDS-PAGE, then subjected to immunoblot analysis. RESULTS: The major amyloid fibril protein was a 29-kD **peptide** which reacted with both anti-lambda- and anti-kappa-light-chain antibodies. CONCLUSION: Amyloids in this particular case of PLCNA are derived from the polyclonal **immunoglobulin light chain** and some cases of PLCNA could be reactive diseases rather than neoplastic ones.

L6 ANSWER 40 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
93270467 EMBASE Document No.: 1993270467. The class I major histocompatibility complex related Fc receptor shows pH- dependent stability differences correlating with immunoglobulin binding and release. Raghavan M.; Gastinel L.N.; Bjorkman P.J.. Division of Biology, Howard Hughes Medical Institute, California Institute of Technology,Pasadena, CA 91125, United States. Biochemistry 32/33 (8654-8660) 1993.
ISSN: 0006-2960. CODEN: BICHAW. Pub. Country: United States. Language: English. Summary Language: English.

AB Maternal immunoglobulin G (IgG) in milk is transported to the bloodstream of newborn rodents via an Fc receptor (FcRn) expressed in the gut. The receptor shows a striking structural similarity to class I major histocompatibility complex (MHC) molecules, being composed of a related heavy chain and the identical light chain (.beta.2-microglobulin). FcRn binds IgG at the pH of milk in the proximal intestine (pH 6.0-6.5) and releases it at the pH of blood (pH .apprx.7.5). We have compared the stability of a **soluble** form of FcRn in these two pH ranges and find that the heterodimer is markedly more stable at the permissive pH for IgG binding. Using the rate of .beta.2m exchange as a correlate of heterodimer stability, we find that exchange is more than 10 times slower at pH 6.1 compared to pH 7.8. Thermal denaturation profiles of FcRn heterodimers at pH 8.0 indicate a two-step, sequential heavy-chain (T(m) = 52 .degree.C) and .beta.2m (T(m) = 67 .degree.C) denaturation. By contrast, at pH 6.0, a single transition is observed, centered at 62 .degree.C, corresponding to denaturation of both chains. The striking difference in stability does not appear to be correlated with the binding of **peptide** as in class I MHC molecules, because analysis of purified FcRn by acid dissociation and sequencing suggests that FcRn is not associated with cellular **peptides**. These results are indicative of pH-dependent conformational changes in the FcRn heterodimer, which may be related to its physiological function.

L6 ANSWER 41 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
93308105 EMBASE Document No.: 1993308105. Priming of cytotoxic T lymphocytes at various stages of ontogeny with transfectoma cells expressing a chimeric Ig heavy chain gene bearing an influenza virus nucleoprotein **peptide**. Kuzu Y.; Kuzu H.; Zaghouani H.; Bona C.. Department of Microbiology, Mount Sinai School of Medicine, One Gustave Levy Place,New York, NY 10029, United States. International Immunology 5/10 (1301-1307) 1993.
ISSN: 0953-8178. CODEN: INIMEN. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB The amino acid residues 147-161 of the nucleoprotein (NP) of influenza virus represent a T cell epitope recognized by cytotoxic T cells (CTLs) in association with K(d) class I molecules. When SP2/0 myeloma B cells are transfected with a chimeric heavy chain gene bearing this particular NP(147-161) **peptide**, they are lysed by CTLs specific for the NP(147-161) **peptide**. Cells that are transfected with this heavy chain chimera and the parental light chain secreted a **soluble** Ig - NP chimera and were also lysed by the CTLs. Herein, we present evidence that transfectoma cells are able to induce in vitro proliferation of NP specific CTL, whereas immobilized Ig- NP chimeras do not. Furthermore, the transfectoma cells expressing the chimeric heavy chain prime NP specific CTLs in adult as well as in newborn mice, while SP2/0 cells coated with NP(147- 161) synthetic **peptide** do not. These data indicate that the NP **peptide** needs to be cleaved from the Ig context in order to be presented to T cells and that only endogenously generated NP **peptide** is immunogenic.

L6 ANSWER 42 OF 49 MEDLINE DUPLICATE 8
93123747 Document Number: 93123747. PubMed ID: 8419479. Role of mouse VH10 and VL gene segments in the specific binding of antibody to Z-DNA, analyzed with recombinant single chain Fv molecules. Brigido M M; Polymenis M; Stollar B D. (Department of Biochemistry, Tufts University School of Medicine, Boston, MA 02111.) JOURNAL OF IMMUNOLOGY, (1993 Jan 15) 150 (2) 469-79. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB A plasmid vector was constructed for the expression of a single chain Fv domain of mouse mAb to Z-DNA (antibody Z22), which is encoded by VH10 and V kappa 10 gene family members along with Dsp2, JH4, and J kappa 4 segments. The vector coded for a PhoA secretion signal, VH segment, flexible **peptide** linker, VL segment, (His)5, and a protein A domain. Unique restriction sites allowed exchange of the segments as cassettes. Bacteria transformed with the vector secreted **soluble** recombinant Fv with specific Z-DNA-binding activity. When the L chain of Z22 was replaced with a library of splenic VL cDNA from a mouse immunized with Z-DNA, only a light chain closely resembling that of the original Z22 (differing at six amino acid positions) yielded Fv with Z-DNA-binding activity. The Fv with this L chain replacement had a lowered affinity, but remained selective for Z-DNA. Replacement of the Z22 H chain with a mixture of 11 VH10-encoded H chains yielded two Z-DNA binding clones, but they bound B-DNA and denatured DNA as well as Z-DNA. The replacement clones indicate the importance of the H chain CDR3 and particular VH-VL combinations in formation of specific antibodies to Z-DNA.

L6 ANSWER 43 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
92096703 EMBASE Document No.: 1992096703. Solution binding of an antigenic **peptide** to a major histocompatibility complex class I molecule and the role of .beta.2-microglobulin. Boyd L.F.; Kozlowski S.; Margulies D.H.. Molecular Biology Section, Laboratory of Immunology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892, United States. Proceedings of the National Academy of Sciences of the United States of America 89/6 (2242-2246) 1992.
ISSN: 0027-8424. CODEN: PNASA6. Pub. Country: United States. Language: English. Summary Language: English.

AB The major histocompatibility complex-encoded class I molecule, a noncovalent dimer of a polymorphic 45-kDa heavy chain and a nonpolymorphic 12-kDa .beta.2-microglobulin (.beta.2m) light chain, binds **peptide** antigen prior to its interaction with T-cell antigen receptors. We report here that the binding in aqueous solution at 37.degree.C of a **soluble** purified murine major histocompatibility complex class I protein, H-2L(s)/(d) (a **soluble** analogue of H-2L(d) consisting of the .alpha.1 and .alpha.2 domains of H-2L(d), the .alpha.3 domain and the C terminus of Q10b), to an antigenic **peptide** is controlled

by the light-chain subunit .beta.2m. Analysis of the equilibrium binding data favors a model in which two classes of **peptide** binding sites exist, the high-affinity class having an equilibrium constant for dissociation, K(H), of 3.7 x 10-7 M and accounting for 12% of the theoretically available sites. Studies of binding in the presence of excess .beta.2m indicate that this increases the concentration of available high-affinity sites. These data are consistent with a ternary model in which high-affinity sites are generated by the interaction of .beta.2m with the **peptide**-binding class I heavy chain.

L6 ANSWER 44 OF 49 MEDLINE DUPLICATE 9

92244340 Document Number: 92244340. PubMed ID: 1315417. Specific low-affinity recognition of major histocompatibility complex plus **peptide** by **soluble** T-cell receptor. Weber S; Traunecker A; Oliveri F; Gerhard W; Karjalainen K. (Basel Institute for Immunology, Switzerland.) NATURE, (1992 Apr 30) 356 (6372) 793-6. Journal code: 0410462. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The T-cell receptor is necessary and sufficient for recognition of **peptides** presented by major histocompatibility complex molecules. Other adhesion molecules, like CD4 or CD8, play an auxiliary role in antigen recognition by T cells. Here we analyse T-cell receptor (TCR) binding using a **soluble** rather than a cell-bound receptor molecule. A TCR-immunoglobulin chimaera is constructed with the variable and the first constant regions of both the TCR alpha- and beta-chains linked to the **immunoglobulin light-chain** constant regions. This **soluble** TCR is expressed, assembled and secreted as an alpha beta heterodimer by a myeloma cell line transfected with the recombinant genes. Furthermore, the **soluble** TCR is biologically active: it specifically inhibits antigen-dependent activation of the relevant T-cell clones and thus discriminates between proper and irrelevant **peptides** presented by major histocompatibility complex molecules.

L6 ANSWER 45 OF 49 MEDLINE DUPLICATE 10

92259412 Document Number: 92259412. PubMed ID: 1582976. Mechanisms of disease: monoclonal immunoglobulin deposition. Amyloidosis, light chain deposition disease, and light and heavy chain deposition disease. Buxbaum J. (Medical Service, New York Department of Veterans Affairs Medical Center, New York.) HEMATOLOGY/ONCOLOGY CLINICS OF NORTH AMERICA, (1992 Apr) 6 (2) 323-46. Ref: 92. Journal code: 8709473. ISSN: 0889-8588. Pub. country: ENGLAND: United Kingdom. Language: English.

AB All forms of MIDD are related to the presence of an expanded clone of B-cell origin that is producing an Ig product, usually, but not exclusively an L-chain, which is predisposed to deposit in tissues, with or without some degree of processing. The nature of the processing is currently unclear, although limited proteolysis is likely to play a major role in most, but not all, patients. Diagnosis is made by the identification, using immunohistochemical techniques, of the monoclonal Ig nature of the deposited material, which may be fibrillar and Congo red-positive (AL and AH), or more amorphous and Congo red-negative (LCDD and LCHDD). Present modalities of therapy are similar or identical to those employed in multiple myeloma, attempting to eliminate the monoclonal cell population responsible for the production of the precursor of the deposited protein. A variety of ancillary therapeutic measures may be employed to treat problems associated with the failure of specific organs produced by the deposition. The details of how the uniformly **soluble** precursor molecule is converted to an essentially insoluble aggregate that compromises the function of the tissue in which it is formed are not yet known. It is still not possible to construct a potential "unified field theory" governing the deposition of intact Igs or their fragments. It is likely, as appears to be the case in other forms of amyloid unrelated to Ig, that many proteins contain, within their

sequence, **peptides** that are capable of forming insoluble beta sheet-like structures. When these **peptides** are isolated from their surrounding molecular environment--either by proteolysis in the test tube, by a mutational change that predisposes them to limited proteolysis; or by a point mutation, deletion, or some other structural modification (as glycosylation), which alters their molecular context without proteolysis--and are present in sufficient concentration, they become less **soluble** under physiologic conditions. It is likely that the site of deposition depends upon the site of synthesis, but to a lesser extent than the protease profile and the physicochemical make-up of the affected tissues. Better understanding of the latter factors is necessary for the development of better modes of treatment.

L6 ANSWER 46 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

92298290 EMBASE Document No.: 1992298290. Variable region differences affect antibody binding to immobilized but not **soluble** antigen. Horgan C.; Brown K.; Pincus S.H.. Lab. of Microbial Structure/Function, Rocky Mountain Laboratories,Hamilton, MT 59840, United States. Human Antibodies and Hybridomas 3/3 (153-157) 1992.
ISSN: 0956-960X. CODEN: HANHEX. Pub. Country: United States. Language: English. Summary Language: English.

AB We have examined the antigen binding characteristics of two chimeric IgG1 antibodies that differ only in the heavy chain variable region. Antibodies 10B and B11 were expressed from two different anti-(Tyr,Glu)-Ala-Lys murine V(H) genes joined to human IgG1 constant region genes in a murine anti- (Tyr,Glu)-Ala-Lys heavy chain loss variant hybridoma. The binding characteristics of the antibodies to (Tyr,Glu)-Ala-Lys and to a **peptide** conjugate, CYYYEEEEY:BSA, were measured in solution and solid phase assays. The antibodies exhibited similar affinities and binding characteristics when assayed in solution assays. However, when we measured binding of antibodies to immobilized antigens, we found that antibody affinity depended on the epitope density in the immobilized immune complexes. The binding of antibody 10B and of B11 to immobilized (Tyr,Glu)-Ala-Lys and to CYYYEEEEY:BSA were similar at high antigen density, but antibody B11 bound less well at lower antigen density. Fab fragments of 10B bound to immobilized (Tyr,Glu)-Ala-Lys and CYYYEEEEY:BSA, but Fab fragments of B11 did not bind to (Tyr,Glu)-Ala-Lys and bound less well to CYYYEEEEY:BSA than 10B Fabs.

L6 ANSWER 47 OF 49 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

1992:214147 Document No.: BA93:114372. THY-1 MULTIMERIZATION IS CORRELATED WITH NEURITE OUTGROWTH. MAHANTHAPPA N K; PATTERSON P H. BIOCHEM. DEP., E. K. SHRIVER CENT. MENTAL RETARDATION, 200 TRAPELO ROAD, WALTHAM, MASS. 02254.. DEV BIOL, (1992) 150 (1), 60-71. CODEN: DEBIAO. ISSN: 0012-1606. Language: English.

AB Thy-1 is abundantly expressed in the vertebrate nervous system. Perturbation studies in vitro suggest that Thy-1 inhibits neurite outgrowth and stabilizes neuronal processes (N. K. Mahanthappa and P. H. Patterson. (1992). Thy-1 involvement in neurite outgrowth: Perturbation by antibodies, phospholipase C, and mutation. Dev. Biol. 150, 47-59). We here report that Thy-1 participates in several types of homophilic interactions, each with differential sensitivity to reduction and boiling. The relative abundance of the multimeric forms of Thy-1 vary with the cell's ability to sprout neurites. Gel filtration chromatography of sympathetic neuron and PC12 cell lysates reveals that Thy-1 immunoreactivity appears in 25-, 45-, and 150-kDa forms. In neurons, Thy-1 immunoreactivity is distributed eqally in all three forms, whereas in PC12 cells, the majority of Thy-1 immunoreactivity is found in the higher molecular weight forms. When PC12 cells are induced to sprout neurites with NGF, the Thy-1 size distribution becomes identical to that of neurons. The three forms of Thy-1 immunoreactivity are likely to be homomultimers of Thy-1 because immunoaffinity-purified, **soluble** Thy-1 also forms complexes similar in size to those found in neuronal

extracts. To test whether Thy-1 multimerization may occur through interactions like those between immunoglobulin heavy and light chains, synthetic **peptides** corresponding to candidate sites for such associations in Thy-1 were tested for their effects on multimerization and neurite outgrowth. One **peptide** increases the amount of monomeric Thy-1 relative to total Thy-1, and promotes outgrowth. These results suggest that multimeric forms of Thy-1 inhibit process outgrowth and neurite sprouting by stabilizing the surface membrane and/or underlying cytoskeleton.

L6 ANSWER 48 OF 49 MEDLINE DUPLICATE 11

91055614 Document Number: 91055614. PubMed ID: 1700755. A stimulatory monoclonal antibody detecting T cell receptor diversity among idiotype-specific, major histocompatibility complex-restricted T cell clones. Bogen B; Lauritzsen G F; Weiss S. (Institute for Immunology, Oslo, Norway.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1990 Oct) 20 (10) 2359-62. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB A panel of independent BALB/c T cell clones responding to a **peptide** of the lambda 2(315) **immunoglobulin light chain** (residues 91-101), in the context of I-Ed, has previously been described. A monoclonal antibody (mAb; GB113) to the T cell receptor (TcR) of one of the clones, 4B2A1 (V alpha 1, J alpha 19; V beta 8.2, D beta 1.1, J beta 1.2) precipitates the alpha/beta heterodimer from 4B2A1. However, GB113 does not bind DO11-10.2 cells bearing a similar alpha/beta heterodimer (V alpha 1.1, J alpha TT11; V beta 8.2, D beta 1.1, J beta 1.1). GB113 does not cross-react with the TcR of the six other clones in the panel. Furthermore, the mAb does not bind polyclonal lambda 2(315)-specific T cell lines except 4.4% of cells of line 4 from which 4B2A1 was cloned. The mAb only binds a negligible number (0.5%) of BALB/c thymocytes and peripheral T cells. Therefore, the epitope detected by GB113 is very rarely expressed on 91-101. lambda 2(315)-specific TcR or on TcR of normal T cells. **Soluble** GB113 induces T cell activation [measured as proliferation and interleukin (IL) 2, IL3 and interferon-gamma production]. GB113-induced T cell activation is enhanced by **soluble** anti-CD4 and anti-Thy-1 mAb.

L6 ANSWER 49 OF 49 MEDLINE DUPLICATE 12

85078227 Document Number: 85078227. PubMed ID: 6334644. Clonotypic surface structure on human T lymphocytes: functional and biochemical analysis of the antigen receptor complex. Reinherz E L; Acuto O; Fabbi M; Bensussan A; Milanese C; Royer H D; Meuer S C; Schlossman S F. IMMUNOLOGICAL REVIEWS, (1984 Oct) 81 95-129. Journal code: 7702118. ISSN: 0105-2896. Pub. country: Denmark. Language: English.

AB Recent studies using cloned antigen-specific T lymphocytes and monoclonal antibodies directed at their various surface glycoprotein components have led to identification of the human T cell antigen receptor as a surface complex comprised of a clonotypic 90KD Ti heterodimer and the monomorphic 20/25KD T3 molecules. Approximately 30,000-40,000 Ti and T3 molecules exist on the surface of human T lymphocytes. These glycoproteins are acquired and fully expressed during late thymic ontogeny, thus providing the structural basis for immunologic competence. The alpha and beta subunits of Ti bear no precursor-product relationship to one another and are encoded by separate genes. The presence of unique **peptides** following proteolysis of different Ti molecules isolated by noncrossreactive anticlonotypic monoclonal antibodies supports the notion that variable regions exist within both the alpha and beta subunits. Moreover, N-terminal amino acid sequencing of the Ti beta subunit shows that it bears homology to the first V-region framework of **immunoglobulin light chains** and represents the product of a gene that rearranges specifically in T lymphocytes. **Soluble** or Sepharose-bound anti-Ti monoclonal antibodies, like physiologic ligand (antigen/MHC), enhanced proliferative responses to

purified IL-2 by inducing a 6-fold increase in surface IL-2 receptor expression. In contrast, only Sepharose-bound anti-Ti or physiologic ligand triggered endogenous clonal IL-2 production and resulted in subsequent proliferation. The latter was blocked by antibodies directed at either the IL-2 receptor or IL-2 itself. These results suggest that induction of IL-2 receptor expression but not IL-2 release occurs in the absence of T3-Ti receptor crosslinking. Perhaps more importantly, the findings demonstrate that antigen-induced proliferation is mediated through an autocrine pathway involving endogenous IL-2 production, release, and subsequent binding to IL-2 receptors.

=> s "Tamm Horsfall glycoprotein"
L8 1684 "TAMM HORSFALL GLYCOPROTEIN"

=> s l8 and derivative
L9 37 L8 AND DERIVATIVE

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10 24 DUP REMOVE L9 (13 DUPLICATES REMOVED)

=> d l10 1-24 cbib abs

L10 ANSWER 1 OF 24 MEDLINE
2001503505 Document Number: 21437095. PubMed ID: 11553518. Localization and functional characterization of Na+/H+ exchanger isoform NHE4 in rat thick ascending limbs. Chambrey R; St John P L; Eladari D; Quentin F; Warnock D G; Abrahamson D R; Podevin R A; Paillard M. (Institut National de la Sante et de la Recherche Medicale Unite 356, Universite Pierre et Marie Curie, 75207 Paris Cedex 06, France.. chambrey@ccr.jussieu.fr) . AMERICAN JOURNAL OF PHYSIOLOGY. RENAL PHYSIOLOGY, (2001 Oct) 281 (4) F707-17. Journal code: 100901990. ISSN: 0363-6127. Pub. country: United States. Language: English.

AB The Na+/H+ exchanger NHE4 was cloned from a rat stomach cDNA library and shown to be expressed predominantly in the stomach and less dramatically in the kidney. The role and precise localization of NHE4 in the kidney are still unknown. A polyclonal antibody against a unique NHE4 decapeptide was used for immunohistochemistry in rat kidney. Simultaneous use of antibodies to **Tamm-Horsfall glycoprotein** and aquaporin-2 or -3 permitted identification of thick ascending limbs and collecting ducts, respectively. The results indicate that NHE4 is highly expressed in basolateral membranes of thick ascending limb and distal convoluted tubule, whereas collecting ducts from cortex to inner medulla and proximal tubules showed weaker basolateral NHE4 expression. Western blot analysis of NHE4 in membrane fractions prepared from the inner stripe of the outer medulla revealed the presence of a 95-kDa protein that was enriched in basolateral membrane vesicles isolated from medullary thick ascending limbs. The inhibition curve of H+-activated (22)Na uptake by 5-(N-ethyl-N-isopropyl)amiloride (EIPA) was consistent with the presence, beyond the EIPA high-affinity NHE1 isoform, of an EIPA low-affinity NHE with apparent half-maximal inhibition of 2.5 microM. Kinetic analyses showed that the extracellular Na+ dependence of NHE4 activity followed a simple hyperbolic relationship, with an apparent affinity constant of 12 mM. Intravesicular H+ activated NHE4 by a positive cooperative mechanism. NHE4 had an unusual low affinity for intravesicular H+ with a half-maximal activation value of pK 6.21. We conclude that NHE4, like NHE1, is expressed on the basolateral membrane of multiple nephron segments. Nevertheless, these two proteins exhibited dramatically different affinities for intracellular H+, suggesting that they may play distinct physiological roles in the kidney.

L10 ANSWER 2 OF 24 EMBASE

2001247725 EMBASE Pathological excretion patterns of urinary proteins in miners highly exposed to dinitrotoluene. Bruning T.; Thier R.; Mann H.; Melzer H.; Brode P.; Dallner G.; Bolt H.M.. Dr. T. Bruning, Ruhr-University, Buerkle-de-la-Camp-Platz 1, D-44789 Bochum, Germany. bruening@bgfa.de. Journal of Occupational and Environmental Medicine 43/7 (610-615) 2001.
Refs: 22.
ISSN: 1076-2752. CODEN: JOEMFM. Pub. Country: United States. Language: English. Summary Language: English.

AB A cohort of 161 underground miners who had been highly exposed to dinitrotoluene (DNT) in the copper-mining industry of the former German Democratic Republic was reinvestigated for signs of subclinical renal damage. The study included a screening of urinary proteins excreted by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), and quantitations of the specific urinary proteins .alpha.(1)-microglobulin and glutathione-S-transferase .alpha. (GST .alpha.) as biomarkers for damage of the proximal tubule and glutathione-S-transferase .pi. (GST .pi.) for damage of the distal tubule. The exposures were categorized semiquantitatively (low, medium, high, and very high), according to the type and duration of professional contact with DNT. A straight dose-dependence of pathological protein excretion patterns with the semiquantitative ranking of DNT exposure was seen. Most of the previously reported cancer cases of the urinary tract, especially those in the higher exposed groups, were confined to pathological urinary protein excretion patterns. The damage from DNT was directed toward the tubular system. In many cases, the appearance of Tamm-Horsfall protein, a 105-kD protein marker, was noted. Data on the biomarkers .alpha.(1)-microglobulin, GST .alpha., and GST .pi. consistently demonstrated a dose-dependent increase in tubular damage, which confirmed the results of screening by SDS-PAGE and clearly indicated a nephrotoxic effect of DNT under the given conditions of exposure. Within the cluster of cancer patients observed among the DNT-exposed workers, only in exceptional cases were normal biomarker excretions found.

L10 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2002 ACS
1999:96091 Document No. 130:165137 Device and method for obtaining clinically significant analyte ratios. Kuo, Hai-Hang; Miller, Carol A.; Wijesuriya, Dayaweere; Yip, Meitak Teresa; Zimmerle, Chris T. (Bayer Corporation, USA). Eur. Pat. Appl. EP 895084 A2 19990203, 18 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 1998-112964 19980713. PRIORITY: US 1997-900586 19970725.

AB Disclosed is a method for detg. the concn. of an analyte in a sample of body fluid. The method involves contacting the body fluid sample with a test strip contg. mobile, labeled, specific binding partner for the analyte. The test fluid, analyte, and any complex formed by interaction of the analyte and labeled specific binding partner flow through the strip by capillarity. The strip contains at least one zone for capture of the labeled specific binding partner and at least one sep. zone for retention of the analyte/labeled specific binding partner complex. By detg. the magnitude of the signal from the detectable label in the capture zone(s) and retention zone(s) and detg. a final response signal by correlating signals using an algorithm and no. of zones chosen in a manner that provides a final response signal best suited for the particular assay, the concn. of the analyte can be detd. with greater precision. A test strip for the detn. of creatinine and deoxypyridinoline contained six distinct areas assembled onto a polystyrene backing of 101.6 X 5.0 mm. Area 1 was a creatinine pad made from Whatman 3 mm filter paper contg. reagents for the colorimetric detn. of creatinine. Area 2 was a buffer pad for buffering the urine samples. Area 3 contained gold sol-labeled anti-deoxypyridinoline antibody. Area 4 contained 3 capture bands of immobilized deoxypyridinoline. Area 5 had an anti-IgG collection band. Area 6 was an absorbant pad. Areas 1 and 2 were dipped into test urine

for 3 s and the strip was placed on the read table of a CLINITEK 50 reflectance spectrometer for anal.

L10 ANSWER 4 OF 24 MEDLINE DUPLICATE 1
1999250941 Document Number: 99250941. PubMed ID: 10231441. Binding of human neutrophils to cell-surface anchored **Tamm-Horsfall glycoprotein** in tubulointerstitial nephritis. Cavallone D; Malagolini N; Serafini-Cessi F. (Department of Experimental Pathology, University of Bologna, Italy.) KIDNEY INTERNATIONAL, (1999 May) 55 (5) 1787-99. Journal code: 0323470. ISSN: 0085-2538. Pub. country: United States. Language: English.

AB BACKGROUND: Human **Tamm-Horsfall glycoprotein** (T-H) is a glycosylphosphatidylinositol-anchored protein exposed at the surface of distal nephron cells, and urinary T-H is the released soluble counterpart. The latter has been implicated in tubulointerstitial nephritis, and the proinflammatory potential has been related to its ability to bind in vitro human neutrophils (PMNs). We have examined the conditions required for the binding of neutrophils to cell-surface anchored T-H and the consequent effects. METHODS: A HeLa cell-line **derivative** permanently transformed with human T-H cDNA and expressing T-H at the cell surface was used throughout the study. The adhesion of PMNs to cells expressing T-H was analyzed by immunofluorescence microscopy before and after the opsonization of cells with anti-T-H antibodies. The oxidative burst induced by adhesion of PMNs to the cells was determined by the activation of myeloperoxidase. Quantitative and qualitative changes in the release of T-H under the adhesion of activated PMNs were determined by dot-blot and Western blot analysis. RESULTS: No binding of neutrophils to cell-surface-anchored T-H was observed. On the contrary, the opsonization of cells with anti-T-H antibodies resulted in a dramatic adhesion of neutrophils. Such an adhesion induced the oxidative burst of PMNs and a large increment in the release of T-H, as well as the release of the slightly faster migrating T-H form, which is normally retained intracellularly. CONCLUSIONS: These results support the notion that, after the autoimmune response, the adhesion of neutrophils to cell-surface T-H contributes to the pathogenesis of tubulointerstitial nephritis, favoring a further accumulation of T-H in the interstitium and inducing the loss of cell integrity via reactive oxygen metabolites generated by activated neutrophils.

L10 ANSWER 5 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
1998359315 EMBASE The abundance of additional N-acetyllactosamine units in N-linked tetraantennary oligosaccharides of human **Tamm-Horsfall glycoprotein** is a donor-specific feature. Van Rooijen J.J.M.; Kamerling J.P.; Vliegenthart J.F.G.. J.F.G. Vliegenthart, Bijvoet Center, Department of Bio-Organic Chemistry, Utrecht University, PO Box 80075, NL-3508 TB Utrecht, Netherlands. Glycobiology 8/11 (1065-1075) 1998.
Refs: 46.
ISSN: 0959-6658. CODEN: GLYCE3. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Previously, treatment of **Tamm-Horsfall glycoprotein** (THp) from different donors with endo-.beta.-galactosidase has been shown to liberate a tetra- and a Sda-active pentasaccharide, concluding the presence of N-linked carbohydrate chains containing additional N-acetyllactosamine units. These type of oligosaccharides were not found in a detailed structure elucidation of the carbohydrate moiety of THp of one male donor, suggesting a donor-specific feature for these type of structures. Therefore, THp was isolated from four healthy male donors and each subjected to endo-.beta.-galactosidase treatment in order to release these tetra- and Sda-active pentasaccharide. Differences were observed in the total amount of released tetra- and Sda-active pentasaccharide of the used donors (42, 470, 478, 718 .mu.g/100

mg THp), indicating that the presence of repeating N-acetyllactosamine units incorporated into the N-glycan moiety of THp is donor specific. Furthermore, a higher expression of the Sda determinant on antennae which display N-acetyllactosamine elongation was observed, suggesting a better accessibility for the .beta.-N-acetylgalactosaminyltransferase. In order to characterize the N-glycans containing repeating N-acetyllactosamine units, carbohydrate chains were enzymatically released from THp and isolated. The tetraantennary fraction, which accounts for more than 33% of the total carbohydrate moiety of THp, was used to isolate oligosaccharides containing additional N-acetyllactosamine units. Five N-linked tetraantennary oligosaccharides containing a repeating N-acetyllactosamine unit were identified, varying from structures bearing four Sda determinants to structures containing no Sda determinant. One compound was used in order to specify the branch location of the additional N-acetyllactosamine unit, and it appeared that only the Gal-6' and Gal-8' residues were occupied by a repeating N-acetyllactosamine unit.

L10 ANSWER 6 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

1998045803 EMBASE Inhibition of myo-inositol transport causes acute renal failure with selective medullary injury in the rat. Kitamura H.; Yamauchi A.; Sugiura T.; Matsuoka Y.; Horio M.; Tohyama M.; Shimada S.; Imai E.; Hori M.. Dr. A. Yamauchi, First Department of Medicine, Osaka University School of Medicine, 2-2, Yamadaoka, Suita, Osaka 565, Japan. atsushi@medone.med.osaka-u.ac.jp. Kidney International 53/1 (146-153) 1998.

Refs: 26.

ISSN: 0085-2538. CODEN: KDYIA5. Pub. Country: United States. Language: English. Summary Language: English.

AB Myo-inositol is a major compatible osmolyte in the renal medulla that is accumulated under hypertonic conditions via the Na+/myo-inositol cotransporter (SMIT). We have recently reported that SMIT is predominantly present in the thick ascending limb of Henle (TAL) and is strongly induced by acute NaCl loading, suggesting an important role of myo-inositol in this nephron segment. In the present study, we sought to examine in vivo effects of inhibition of myo-inositol transport using a transport inhibitor, 2-O, C- methylene-myo-inositol (MMI). Intraperitoneal injection of MMI caused acute renal failure in the rats. Serum creatinine and urea nitrogen were significantly increased 12 hours after MMI injection. Morphologic study revealed that the tubular cells were extensively injured in the outer medulla. A considerable number of the tubular cells were injured in the cortex as well. Immunohistochemical study for Tamm-Horsfall protein (THP), which was used for identification of the TAL cells, showed that THP-positive cells were predominantly injured. The tubular injury apparently appeared to worsen when high concentration of NaCl was injected with MMI. Administration of myo-inositol prevented acute renal failure and improved the tubular injury after MMI injection. Furthermore, supplementation of betaine, another osmolyte in the TAL cells, partially prevented the toxic effects of MMI. These results suggest that myo-inositol play a crucial role in the TAL regarding osmoregulation of the cells.

L10 ANSWER 7 OF 24 SCISEARCH COPYRIGHT 2002 ISI (R)

97:336837 The Genuine Article (R) Number: WV918. Synthesis of two analogues of the Sd(a) determinant. Replacement of the sialic acid residue by a sulfate or a carboxymethyl group. vanSeeventer P B; Corsten M A; Sanders M P; Kamerling J P; Vliegenthart J F G (Reprint). UNIV UTRECHT, BIJVOET CTR, DEPT BIOORGAN CHEM, POB 80075, NL-3508 TB UTRECHT, NETHERLANDS (Reprint); UNIV UTRECHT, BIJVOET CTR, DEPT BIOORGAN CHEM, NL-3508 TB UTRECHT, NETHERLANDS. CARBOHYDRATE RESEARCH (21 APR 1997) Vol. 299, No. 3, pp. 171-179. Publisher: ELSEVIER SCI LTD. THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, OXON, ENGLAND OX5 1GB. ISSN: 0008-6215. Pub. country: NETHERLANDS. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Two analogues of the Sd(a) determinant tetrasaccharide have been synthesized in order to investigate the physiological role of this carbohydrate moiety. These saccharides, having two different anionic substitutes for the sialic acid residue, are: beta-D-GalpNAc-(1 --> 4)-3-O-SO3H-beta-D-Galp-(1 --> 4)-beta-D-GlcpNAc-(1 --> 0)(CH2)(5)NH2 and beta-D-GalpNAc-(1 --> 4)-3-O-CH2COOH-beta-D-Galp-(1 --> 4)-beta-D-GlcpNAc-(1 --> 0)(CH2)(5)NH2. 5-Azidopentyl (2,6-di-O-benzyl-beta-D-galactopyranosyl)-(1 --> 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-beta-D-glucopyranoside served as a general building block. The trisaccharides were obtained after prior selective derivatization of HO-3' of the disaccharide **derivative** via a dibutyltin oxide mediated reaction, followed by coupling at HO-4' with 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-beta-D-galactopyranosyl trichloroacetimidate, and processing of the formed trisaccharide **derivatives** into their free forms.

L10 ANSWER 8 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
1998169195 EMBASE Interactions of renal cytochrome P450 (CYP), angiotensin (AII) and tumor necrosis factor-alpha (TNF): Implications for ion transport. McGiff J.C.; Ferreri N.R.; Escalante B.A.; Carroll M.A.. J.C. McGiff, New York Medical College, Department of Pharmacology, Valhalla, NY 10595, United States. Advances in Experimental Medicine and Biology 433/-(103-107) 1997.
Refs: 10.
ISSN: 0065-2598. CODEN: AEMBAP. Pub. Country: United States. Language: English.

L10 ANSWER 9 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
96042668 EMBASE Document No.: 1996042668. The effects of quinolones on the adherence of type-1 fimbriated Escherichia coli to mannosylated agarose beads. Breines D.M.; Burnham J.C.. Department of Medicine, Infectious Diseases Unit, Massachusetts General Hospital, Fruit Street,Boston MA 02114, United States. Journal of Antimicrobial Chemotherapy 36/6 (911-925) 1995.
ISSN: 0305-7453. CODEN: JACHDX. Pub. Country: United Kingdom. Language: English. Summary Language: English.
AB Bacterial adherence is reported to be antagonized by several classes of antibiotics including quinolones, .beta.-lactams and tetracyclines, based primarily on in-vitro studies in which bacterial cells are exposed to antimicrobials, incubated in the presence of uroepithelial cells (UECs) and assessed for adherence by light microscopy. Some problems associated with the use of this approach, include low sensitivity, high variability and, in the case of adherence of mannose-sensitive Escherichia coli interference by mannose-containing uromucoid. To avoid these problems, mannosylated agarose beads (MABs) were used as a model for UECs. Adherence of E. coil strain AAEC356, which is constitutive for type-1 fimbrial expression, was maximal with 3 x 104 beads/mL and 1 x 108 bacterial cells/mL co-incubated for 35 min at 37.degree.C. Those bacterial cultures showed 40-60% adherence to MABs but only 4-10% adherence to UECs. This study reports a novel method to detect mannose-sensitive bacterial adherence, using MABs, in order to determine the effects of quinolones, cefdinir and tetracycline on E. coil adherence. Cefdinir and the quinolones ciprofloxacin, enoxacin and PD 131628 caused significant reductions in the adherence of AAEC356 to UECs at concentrations equivalent to 1/2 x MIC, while up to 1 x MIC of these antibiotics had no significant effect on adherence to MABs. A direct comparison of UEC to MAB-based techniques showed that PD131628, at concentrations equivalent to 1/16 x, 1/4 x, 1/2 x and 1 x MIC, had no effect on bacterial adherence to MABs, while reductions of 34%, 38%, 87% and 85% respectively were seen in adherence to UECs. The anti-adherent effect mediated by quinolones may not therefore be related to the specific interaction between type-1 fimbriae and mannosylated receptors. While quinolones and cefdinir had no effect on overall bacterial adherence to MABs, there was a decrease in the ability

of a-methyl-D-mannoside (.alpha.-MM) to inhibit competitively this adherence. Concurrent exposure of PD131628 or cefdinir with tetracycline prevented this, suggesting that protein synthesis is required for this effect.

L10 ANSWER 10 OF 24 SCISEARCH COPYRIGHT 2002 ISI (R)
95:757795 The Genuine Article (R) Number: TC156. THE STRUCTURE OF THE EXOPOLYSACCHARIDE PRODUCED BY LACTOBACILLUS-HELVETICUS-766. ROBIJN G W; THOMAS J R; HAAS H; VANDENBERG D J C; KAMERLING J P (Reprint); VLIEGENTHART J F G. UNIV UTRECHT, DEPT BIOORGAN CHEM, BIJVOET CTR, POB 80075, 3508 TB UTRECHT, NETHERLANDS (Reprint); UNIV UTRECHT, DEPT BIOORGAN CHEM, BIJVOET CTR, 3508 TB UTRECHT, NETHERLANDS; UNILEVER RES LABS VLAARDINGEN, 3130 AC VLAARDINGEN 3130, NETHERLANDS. CARBOHYDRATE RESEARCH (16 OCT 1995) Vol. 276, No. 1, pp. 137-154. ISSN: 0008-6215. Pub. country: NETHERLANDS. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The exopolysaccharide produced by Lactobacillus helveticus 766 in skimmed milk was found to be composed of D-glucose and D-galactose in a molar ratio of 2:1. Linkage analysis and 1D/2D NMR studies (H-1 and C-13) performed on the native polysaccharide, and on oligosaccharides obtained from a partial acid hydrolysate, showed the polysaccharide to consist of hexasaccharide repeating units with the following structure:
[GRAPHICS]
UP>31</SUP>P) studies the polysaccharide was shown to be composed of repeating units with the following structure:
[GRAPHICS]
tetra-O-acetyl-2-epi-streptozotocin (the acetylated alpha-mannosamine epimer of streptozotocin). Administration of 50 mg/kg/day X 5 to leukemia L1210-bearing DBA/2Ha mice resulted in 5/5 35-day survivors. Neutralization of 1,3,3,6-tetra-O-acetyl-2-amino-2-deoxy-alpha-D-mannopyranose oxalate under aqueous conditions led to 2-acetamido-1,4,6-tri-O-acetyl-2-deoxy-alpha-D-mannopyranose, the oxidation of which gave 2-acetamido-4,6-di-O-acetyl-1,5-anhydro-2-deoxy-D-erythro-hex-1-en-3-ulose. This agent demonstrated an IC50 of 25 mu M with a murine L1210 cell culture. Administration of 100 mg/kg/day X 5 resulted in 42% ILS in DBA/2 mice with ip L1210 leukemia. Several other nonacetylated **derivatives** were also prepared by direct N-acylation, producing, for example, fluorescently tagged N-dansylmannosamine.

L10 ANSWER 11 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
94276625 EMBASE Document No.: 1994276625. A 92-kDa human immunostimulatory protein. Fontan E.; Briend E.; Saklani-Jusforgues H.; D'Alayer J.; Vandekerckhove J.; Fauve R.M.. Unite d'Immunophysiologie Cellulaire, Institut Pasteur, 25 rue du Dr. Roux,75724 Paris Cedex 15, France. Proceedings of the National Academy of Sciences of the United States of America 91/18 (8353-8357) 1994.
ISSN: 0027-8424. CODEN: PNASA6. Pub. Country: United States. Language: English. Summary Language: English.
AB We purified to apparent homogeneity a human urinary glycoprotein of 92 kDa (HGP.92) that, administered intravenously at 250 .mu.g/kg, fully protected mice against a lethal inoculum of Listeria monocytogenes. Since HGP.92 protected scid mice, which lack B and T lymphocytes, this increased resistance to Listeria did not appear to be lymphocyte mediated. Furthermore, inflammatory macrophages incubated with 6 nM HGP.92 inhibited the growth of Lewis carcinoma cells in vitro. These two activities appeared to depend on an oligosaccharide moiety, as they were lost after N-Glycanase treatment of HGP.92. Thus, the biological activity of HGP.92 was in some way related to a glycan moiety.

L10 ANSWER 12 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
94177335 EMBASE Document No.: 1994177335. Studies on glycoprotein-derived carbohydrates. Vliegenthart J.F.G.. Department of Bio-Organic Chemistry, Bijvoetcenter, Utrecht University, PO Box 80.075,NI-3508 TB Utrecht,

Netherlands. Biochemical Society Transactions 22/2 (370-373) 1994.
ISSN: 0300-5127. CODEN: BCSTB5. Pub. Country: United Kingdom. Language: English.

L10 ANSWER 13 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
93272440 EMBASE Document No.: 1993272440. Reconsideration of the development of the distal tubule of the human kidney. Howie A.; Smithson N.; Rollason T.P.. Department of Pathology, The Medical School,Birmingham B15 2TT, United Kingdom. Journal of Anatomy 183/1 (141-147) 1993.
ISSN: 0021-8782. CODEN: JOANAY. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB The human kidney develops from 2 embryonic tissues, the ureteric bud and the metanephric blastema. The site in the adult renal distal tubule corresponding to the junction between these tissues has never been established unequivocally and is usually said to be the union between the collecting duct and the connecting piece, based on microdissection evidence. We have examined kidneys from 21 human fetuses of various ages using an immunohistological method for substances related to the ABO blood group system, various cytokeratins including those detected by the monoclonal antibody PKK2, and Tamm-Horsfall protein. The ureteric bud and connecting piece expressed the type 1 precursor chain of ABO antigens mostly early in gestation, the H antigen of the ABO system mostly later in gestation, and cytokeratins detected by PKK2. The induced nephrons after the S-shaped body stage expressed Tamm-Horsfall protein. In the adult renal tubule, distal from the macula densa, it was already known that there is a sharp junction between the segment expressing Tamm-Horsfall protein and the more distal segment that expresses the H antigen and cytokeratins detected by PKK2. The finding that the ureteric bud and connecting piece express the same antigens as this segment while the S-shaped body eventually expresses Tamm-Horsfall protein is consistent with the concept that (1) the connecting piece arises from the ureteric bud, not the S-shaped body, and (2) the junction of ureteric bud **derivatives** and metanephric blastema **derivatives** is on the distal side of the macula densa at the distal end of Tamm-Horsfall staining.

L10 ANSWER 14 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
92282011 EMBASE Document No.: 1992282011. Specificity of the sialic acid-binding lectin from the snail Cepaea hortensis. Brossmer R.; Wagner M.; Fischer E.. Institute of Biochemistry II, University of Heidelberg, Im Neuenheimer Feld 328,W-6900 Heidelberg, Germany. Journal of Biological Chemistry 267/13 (8752-8756) 1992.
ISSN: 0021-9258. CODEN: JBCHA3. Pub. Country: United States. Language: English. Summary Language: English.

AB The specificity of the sialic acid-binding lectin from the snail Cepaea hortensis, purified by affinity chromatography on fetuin-Sepharose, was studied by hemagglutination inhibition assay applying 32 sialic acid **derivatives** and 14 glycoproteins. 2-.alpha.-Methyl-9-O-acetyl-NeuAc was the most potent inhibitor, followed closely by 2-.alpha.-methyl-NeuAc and 2-.alpha.-benzyl- NeuAc. An axially orientated carboxyl group is a prerequisite for maximal lectin-sugar binding. Neither size nor polarity of the .alpha.-anomeric substituent significantly influenced inhibition potency. An intact sialic acid N-acetyl group is essential for optimal lectin-sugar interaction. The trihydroxypropyl side chain also is of great importance. However, a bulky hydrophobic substituent at the side chain like a 9-O-tosyl residue did not decrease binding to the lectin. The lectin did not distinguish between NeuAc.alpha.2.fwdarw.3Gal.beta.1.fwdarw.4Glc and NeuAc.alpha.2.fwdarw.6Gal.beta.1.fwdarw.4Glc. Among other sugars tested, only N-acetylglucosamine showed inhibition, although 50-fold less. The most potent glycoprotein inhibitors were those carrying O-chains only or preferentially, as ovine submaxillary mucin, bovine submaxillary mucin, and glycophorin A. Tamm-Horsfall protein was an exception being a strong

inhibitor, although carrying only N-chains. Asialoglycoproteins were inactive. Glycoproteins containing the NeuAc.alpha.2.fwdarw.3Gal sequence inhibited the lectin as well as those with NeuAc.alpha.2.fwdarw.6GalNAc. From the results a model of the lectin's binding site for sialic acid is suggested.

L10 ANSWER 15 OF 24 MEDLINE DUPLICATE 2
93064846 Document Number: 93064846. PubMed ID: 1437276. Adhesion of Trichomonas vaginalis to plastic surfaces: requirement for energy and serum constituents. Gold D; Ofek I. (Department of Human Microbiology, Sackler Faculty of Medicine, Tel-Aviv University, Israel.) PARASITOLOGY, (1992 Aug) 105 (Pt 1) 55-62. Journal code: 0401121. ISSN: 0031-1820. Pub. country: ENGLAND: United Kingdom. Language: English.
AB The ability of Trichomonas vaginalis to adhere to plastic surfaces in the presence of various agents and under different growth conditions was examined in wells of microtitre plates containing unsupplemented TYI medium or the same, with various supplements. Following incubation, the wells were thoroughly washed and adhesion was determined by microscopic counting of the adherent organisms. There was no detectable adhesion in the absence of both serum and carbohydrate. Optimal adhesion (about 10-20% of the total number of parasites) was obtained throughout the growth curve in culture media supplemented with either serum or serum Cohn fractions IV-I (rich in alpha-globulin) or IV-4 (rich in alpha + beta-globulin) and 25 mM glucose, maltose or fructose, but not in plates pre-coated with the Cohn fractions. Cohn fraction II + III (rich in beta + gamma-globulin) moderately enhanced adhesion while Cohn fractions II (rich in gamma-globulin) or V (albumin), fibronectin, **Tamm-Horsfall glycoproteins** and polylysine were without effect. Non-metabolizable sugars (methyl **derivatives** of glucose, mannose or fucose) did not support growth, but, surprisingly, enhanced adhesion. At 4 degrees C, the trichomonads were not able to adhere and pre-adherent organisms detached from the plastic surface. Optimal adhesion was obtained at a pH range of 6.5-7.5 but was already detectable at pH 5.5. Cytochalasin E markedly suppressed adhesion.(ABSTRACT TRUNCATED AT 250 WORDS)

L10 ANSWER 16 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
91322550 EMBASE Document No.: 1991322550. Role of the sodium ion in acute renal failure. Swan S.K.; Bennett W.M.. Division of Nephrology, Oregon Health Sciences University, 3181 Sam Jackson Park Road, Portland, OR 97201, United States. Mineral and Electrolyte Metabolism 17/2 (89-99) 1991.
ISSN: 0378-0392. CODEN: MELMDI. Pub. Country: Switzerland. Language: English. Summary Language: English.

L10 ANSWER 17 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
91139795 EMBASE Document No.: 1991139795. Determination of urinary Tamm-Horsfall protein by ELISA using a maleimides method for enzyme-antibody conjugation. Uto I.; Ishimatsu T.; Hirayama H.; Ueda S.; Tsuruta J.; Kambara T.. Department of Urology, Inst. for Medical Immunology, Kumamoto Univ. Medical School,Kumamoto, Japan. Journal of Immunological Methods 138/1 (87-94) 1991.
ISSN: 0022-1759. CODEN: JIMMBG. Pub. Country: Netherlands. Language: English. Summary Language: English.
AB A method for enzyme-antibody conjugation using a new maleimide **derivative** as coupling reagent has been developed. Since a monomeric conjugate of horseradish peroxidase and Fab' antibody could be readily prepared with high efficiency and reproducibility, the enzyme activity and antigen-binding activity were well preserved and nonspecific staining was greatly reduced. The conjugate is suitable for use in both ELISA procedures and immunohistochemistry. Using both methods we examined the pathophysiological significance of Tamm-Horsfall protein (THP) and the present study describes the ELISA method to quantify urinary THP using the

new method with rabbit anti-THP antibody. A low concentration (0.04 M) of urea added to the urine samples increased the linearity of the standard curve and the sensitivity of the assay, permitting the detection of as little as 20 ng/ml THP. Freezing and thawing the urine resulted in variable or lower values of THP concentration. THP concentrations in urine as determined by ELISA were stable for at least one month after -70.degree.C storage, but not after -30.degree.C storage. There was no correlation between THP concentrations in 24 h urine samples and the morning urine of the same patient. These result suggest that it is essential to use fresh or -70.degree.C stored 24 h urine samples with added urea (0.04 M) for the determination of THP concentrations in urine by the present enzyme-antibody conjugation method. The THP concentration in normal 24 h urine of young children was found to be less than 51.8 mg/g Cr.

L10 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2002 ACS

1991:182855 Document No. 114:182855 Pregnancy-associated changes in oligomannose oligosaccharides of human and bovine uromodulin (**Tamm -Horsfall glycoprotein**). Smagula, Rosalita M.; Van Halbeek, Herman; Decker, Jean M.; Muchmore, Andrew V.; Moody, Charles E.; Sherblom, Anne P. (Dep. Biochem., Univ. Maine, Orono, ME, 04469, USA). Glycoconjugate J., 7(6), 609-24 (English) 1990. CODEN: GLJOEW. ISSN: 0282-0080.

AB The urinary glycoprotein uromodulin (**Tamm-Horsfall glycoprotein**) has previously been shown to exhibit a pregnancy-assocd. ability to inhibit antigen-specific T cell proliferation, and this activity is assocd. with a carbohydrate moiety. Here, the Man6(7)GlcNAc2-R glycopeptides derived from uromodulin inhibited antigen-specific T cell proliferation by 50% at 0.2-2 .mu.M. Also, pregnancy-assocd. inhibitory activity is described in a 2nd species. The oligomannose profile of **Tamm-Horsfall glycoprotein** (nonpregnant) was compared with that of uromodulin (pregnant) derived from both human and bovine sources. Surprisingly, there was a pregnancy-assocd. decrease in the total content of oligomannose chains due predominantly to a redn. in Man5GlcNAc2-R and Man6GlcNAc2-R. Man7GlcNAc2-R, which did not decrease with pregnancy, comprised a significantly greater proportion of the total oligomannose chains in pregnant vs. nonpregnant samples from both species (human; 34.6% vs. 25.9%: bovine; 14.4% vs. 7.2%).

L10 ANSWER 19 OF 24 MEDLINE

91134039 Document Number: 91134039. PubMed ID: 2284219. Renal and gastrointestinal tolerability of lornoxicam, and effects on haemostasis and hepatic microsomal oxidation. Warrington S J; Lewis Y; Dawnay A; Johnston A; Kovacs I B; Lamb E; Ravic M. (Charterhouse Clinical Research Unit Limited, London, UK.) POSTGRADUATE MEDICAL JOURNAL, (1990) 66 Suppl 4 S35-40. Journal code: 0234135. ISSN: 0032-5473. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Three separate studies were carried out to assess the renal and gastrointestinal tolerability of lornoxicam, and its effects on haemostasis and hepatic microsomal oxidation. Haemostasis and hepatic microsomal oxidation. Six men and 6 women had salivary antipyrine half-life determined before and on the last day of 14 days' treatment with lornoxicam 4 mg twice daily. Haemostasis, coagulation and thrombolysis were assessed ex vivo using a haemostatometer before and on Day 14 of lornoxicam treatment. Lornoxicam 4 mg twice daily for 14 days had no significant influence on antipyrine elimination half-life or haemostasis, coagulation and thrombolysis. Renal tolerability. Three groups of 8 healthy young men received respectively 4, 6 and 8 mg lornoxicam twice daily by mouth for 22 days. Nephrotoxicity studies on serum and urine were done repeatedly before, during and after lornoxicam treatment. Serum and urine creatinine, serum **Tamm-Horsfall glycoprotein** (THG), and urine n-acetylglucosaminidase (NAG), THG

and retinol binding protein (RBP) concentrations showed sporadic values outside the laboratory reference range, but these were not in any subject temporally related to drug treatment and were unrelated to dose. Urine microscopy was unremarkable. Thus this study yielded no evidence that lornoxicam has any nephrotoxic effects in healthy young men receiving doses up to 8 mg twice daily for 22 days. Gastrointestinal blood loss and endoscopy. The gastrointestinal effects of lornoxicam 4 mg, indomethacin 50 mg or placebo twice daily for 29 days were evaluated in 45 healthy men. After an initial endoscopic examination, subjects underwent 51Cr red cell labelling. Complete daily faecal collections were then made from Days 6-12, 20-26 and 34-40. Treatments were given from Days 13-41. Endoscopy was repeated 4-8 h after the last dose of medication. Faecal blood loss during lornoxicam treatment was greater than placebo and less than indomethacin, but within- and between-subject variability was such that the differences were not statistically significant. Endoscopic findings were normal in most subjects before and after all 3 treatments.

L10 ANSWER 20 OF 24 MEDLINE DUPLICATE 3
81210069 Document Number: 81210069. PubMed ID: 7237482. Isolation and characterisation of glycopeptides from digests of human **Tamm-Horsfall glycoprotein**. Afonso A M. CARBOHYDRATE RESEARCH, (1981 Mar 2) 89 (2) 309-19. Journal code: 0043535. ISSN: 0008-6215. Pub. country: Netherlands. Language: English.

AB Glycopeptides were isolated from pronase digests of human **Tamm-Horsfall glycoprotein** and its asialo **derivative**. The carbohydrate moiety of the major glycopeptide preparation isolated from the former digests had an apparent molecular weight of 4300, and those of two glycopeptides isolated from the latter digests had molecular weights of 3600 and 2300. These data, together with the compositions of the glycopeptides, indicate that the **Tamm-Horsfall glycoprotein** has at least five asparagine residues substituted by complex carbohydrate moieties, three being of one type, relatively rich in galactose, and two containing more sialic acid but less galactose. A small amount of a mannose-rich glycopeptide was also recovered from the digests of the **Tamm-Horsfall glycoprotein**.

L10 ANSWER 21 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 4
78409901 EMBASE Document No.: 1978409901. Stimulation of human peripheral blood lymphocytes by Tamm-Horsfall urinary glycoprotein. Hunt J.S.; McGiven A.R.. Dept. Pathol., Christchurch Clin. Med., Christchurch, New Zealand. Immunology 35/2 (391-395) 1978.
CODEN: IMMUAM. Pub. Country: United Kingdom. Language: English.

AB THP, prepared by salt precipitation of pooled urine from normal individuals, stimulated purified human peripheral blood lymphocytes (PBL) to undergo blastoid transformation. The response was measured by tritiated thymidine uptake into DNA after 6 days in culture. Several batches of THP stimulated, in varying degrees, all samples of PBL tested and the response approached that seen with the mitogens phytohaemagglutinin (PHA), Concanavalin A (Con A) and pokeweed mitogen (PWM) after 4 days in culture. The response usually exceeded that seen after 6 days with tuberculin purified protein **derivative** (PPD) in Mantoux positive lymphocyte donors.

L10 ANSWER 22 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 5
74059700 EMBASE Document No.: 1974059700. Kinetic studies on the acid hydrolysis of the methyl ketoside of unsubstituted and O acetylated N acetylneuraminic acid. Neuberger A.; Ratcliffe W.A.. Dept. Chem. Pathol., St. Mary's Hosp. Med. Sch., London, United Kingdom. Biochemical Journal 133/4 (623-628) 1973.
CODEN: BIJOAK. Language: English.

AB The hydrolysis of the model compound 2 O methyl 4,7,8,9 tetra O acetyl N acetyl .alpha. D neuraminic acid by acid and neuraminidase (Vibrio cholerae) closely resembled that of the O acetylated sialic acid residues

of rabbit **Tamm Horsfall glycoprotein**. This confirmed that O acetylation was responsible for the unusually slow rate of acid hydrolysis of O acetylated sialic acid residues observed in rabbit **Tamm Horsfall glycoprotein** and their resistance to hydrolysis by neuraminidase. The first order rate constant of hydrolysis of 2 methyl N acetyl .alpha. D neuraminic acid by 0.05 M H2SO4 was 56 fold greater than that of 2 O methyl 4,7,8,9 tetra O acetyl N acetyl .alpha. D neuraminic acid. Kinetic studies have shown that in the pH range 1.00-3.30, the observed rate of hydrolysis of 2 methyl N acetyl .alpha. D neuraminic acid can be attributed to acid catalysed hydrolysis of the negatively charged CO2- form of the methyl ketoside.

L10 ANSWER 23 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 6
74146487 EMBASE Document No.: 1974146487. Morphological and conformational studies of Tamm Horsfall urinary glycoprotein. Robinson J.P.; Puett D.. Dept. Microbiol., Vanderbilt Univ., Nashville, Tenn. 37232, United States. Archives of Biochemistry and Biophysics 159/2 (615-621) 1973. CODEN: ABBIA4. Language: English.

AB The circular dichroic properties of normal and cystic fibrotic Tamm Horsfall urinary glycoproteins, and the asialo **derivatives** (ca. 80% removal of sialic acid with neuraminidase) were studied. There was no evidence of .alpha. helicity in Tamm Horsfall urinary glycoprotein, but the results do indicate a significant amount of .beta. structure. The circular dichroic spectra of normal and cystic fibrotic Tamm Horsfall urinary glycoproteins and the asialo **derivatives** were identical, suggesting that there is no major difference in the ordered secondary structure of Tamm Horsfall urinary glycoprotein in cystic fibrosis (relative to normal Tamm Horsfall urinary glycoprotein), and that sialic acid exerts no major effect on the .beta. structure. Also, the circular dichroic spectrum of Tamm Horsfall urinary glycoprotein was not affected by Ca2+ at concentrations just below that required for gel formation. Electron microscopic studies reveal the presence of a supramolecular helical structure arising from subunit interactions. This structure was characterized by a repeat of 120-130 .ANG. and a minimal helix diameter of about 40 .ANG., although this value varied depending on the number of interacting helices. The helical structure was observed for normal, cystic fibrotic, and asialo **derivatives** of Tamm Horsfall urinary glycoproteins, and was independent of added Ca2+. Guanidine hydrochloride treatment followed by dialysis irreversibly destroyed this supramolecular helical structure, but the .beta. structure was partially restored, as indicated by the circular dichroic spectrum. The Ca2+ mediated gel formation was inhibited in asialo Tamm Horsfall urinary glycoprotein.

L10 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2002 ACS
1973:12897 Document No. 78:12897 Acid and enzymic hydrolysis of O-acetylated sialic acid residues from rabbit **Tamm-Horsfall glycoprotein**. Neuberger, A.; Ratcliffe, Wendy A. (Dep. Chem. Pathol., St. Mary's Hosp. Med. Sch., London, Engl.). Biochem. J., 129(3), 683-93 (English) 1972. CODEN: BIJOAK.

AB Rabbit **Tamm-Horsfall glycoprotein** and bovine submaxillary glycoprotein contained sialic acid (I) residues which were resistant to std. conditions of acid hydrolysis and treatment with neuraminidases of Vibrio comma and Clostridium perfringens. This was attributed to the presence of O-acetylated I, since the removal of the OAc groups with mild alkali normalized sialic acid release by acid or enzymic hydrolysis. There were on the av. 2 OAc groups per I residue located on the polyhydroxy side chain or on C-4 and C-8. The effect of O-acetylation of the side chain on the rate of acid-catalyzed hydrolysis of I residues is discussed.

=> s romoduline
L11 0 ROMODULINE

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=> s uromoduline
L12           0 UROMODULINE

=> s "uromoduline"
L13           0 "UROMODULINE"

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L14        1721 (REDEGELD F?/AU OR KRANEVELD A?/AU OR NIJKAMP F?/AU)

=> s l14 and "LC binding peptide"
L15           0 L14 AND "LC BINDING PEPTIDE"

=> s l14 and light chain immunoglobulin
L16           1 L14 AND LIGHT CHAIN IMMUNOGLOBULIN

=> d l16 cbib abs

L16  ANSWER 1 OF 1  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1999:167675  Document No.: PREV199900167675. A novel pathway for
     antigen-specific activation of mast cells. Redegeld, Frank A.;
     Heijdra, Bianca H.; Garssen, Johan; Nijkamp, Frans P.. Dep.
     Pharmacol. and Pathophysiol., UIPS, Utrecht Univ., Sorbonnelaan 16, 3584
     CA Utrecht Netherlands. FASEB Journal, (March 12, 1999) Vol. 13, No. 4
     PART 1, pp. A334. Meeting Info.: Annual Meeting of the Professional
     Research Scientists for Experimental Biology 99 Washington, D.C., USA
     April 17-21, 1999 ISSN: 0892-6638. Language: English.


=> s "AHWSGHCCL"
L17           5 "AHWSGHCCL"

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L18            1 DUP REMOVE L17 (4 DUPLICATES REMOVED)

=> d l18 cbib abs

L18  ANSWER 1 OF 1     MEDLINE                              DUPLICATE 1
97197581  Document Number: 97197581.     PubMed ID: 9045877.   Localization of a
     single binding site for immunoglobulin light chains on human Tamm-Horsfall
     glycoprotein. Huang Z Q; Sanders P W. (Department of Veterans Affairs
     Medical Center, Birmingham, Alabama 35233, USA. ) JOURNAL OF CLINICAL
     INVESTIGATION, (1997 Feb 15) 99 (4) 732-6.  Journal code: 7802877. ISSN:
     0021-9738. Pub. country: United States. Language: English.
AB   Cast nephropathy is a severe complication of multiple myeloma. Binding of
     filtered monoclonal light chains (LC) with Tamm-Horsfall glycoprotein
     (THP) triggers heterotypic aggregation of these two proteins to form casts
     in the distal nephron of the kidney. To localize the LC binding site on
     THP, human THP was deglycosylated and underwent limited trypsin digestion
     in the presence or absence of a nephrotoxic LC known to bind THP. A
     29.6-kD band was protected from trypsin digestion by the addition of LC.
     NH2-terminal amino acid sequence and amino acid analyses revealed this
     band was located between the 6th and 287th amino acid residues of THP. Six
     peptides located within this 29.6-kD fragment were synthesized and used as
     potential inhibitors of binding or aggregation of five different
     nephrotoxic LCs with THP. Peptide AHWSGHCCL (from amino acid 225
     to 233) completely inhibited binding and aggregation of these proteins.
     Optimal inhibition required a cystine residue in this peptide. Truncation
     experiments demonstrated the entire sequence was necessary for ideal
     inhibition and the histidine residue explained the effects of pH on
     binding. These studies provided a basis for further study of LC-THP
     interaction and a potential approach toward the prevention of cast
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nephropathy.

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NEWS 6	Mar 08	Gene Names now available in BIOSIS
NEWS 7	Mar 22	TOXLIT no longer available
NEWS 8	Mar 22	TRCTHERMO no longer available
NEWS 9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
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               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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L1          463 UROMODULIN

=> s l1 adn peptide
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nested terms that are not separated by a logical operator.

=> s l1 and peptide
L2           47 L1 AND PEPTIDE

=> s l2 and immunoglobulin light chain
L3            1 L2 AND IMMUNOGLOBULIN LIGHT CHAIN

=> d l3 cbib abs
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L3 ANSWER 1 OF 1 SCISEARCH COPYRIGHT 2002 ISI (R)
93:749146 The Genuine Article (R) Number: ML643. BENCE-JONES PROTEINS BIND TO A COMMON **PEPTIDE** SEGMENT OF TAMM-HORSFALL GLYCOPROTEIN TO PROMOTE HETEROTYPIC AGGREGATION. HUANG Z Q; KIRK K A; CONNELLY K G; SANDERS P W (Reprint). UNIV ALABAMA, DEPT MED, DIV NEPHROL, CTR NEPHROL RES & TRAINING, 642 LYONS HARRISON RES BLDG, BIRMINGHAM, AL, 35292; UNIV ALABAMA, DEPT PHYSIOL, DIV NEPHROL, CTR NEPHROL RES & TRAINING, BIRMINGHAM, AL, 35292; UNIV ALABAMA, DEPT BIOSTAT & BIOMATH, DIV NEPHROL, CTR NEPHROL RES & TRAINING, BIRMINGHAM, AL, 35292; VET AFFAIRS MED CTR, BIRMINGHAM, AL, 35292. JOURNAL OF CLINICAL INVESTIGATION (DEC 1993) Vol. 92, No. 6, pp. 2975-2983. ISSN: 0021-9738. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Bence Jones proteins (BJPs) are the major pathogenic factor causing cast nephropathy (''myeloma kidney'') by coaggregation with Tamm-Horsfall glycoprotein (THP). Understanding the interaction between these proteins is therefore important in developing treatment strategies to prevent renal failure from cast formation in multiple myeloma. We developed an enzyme-linked immunoassay to examine this phenomenon. Five different human BJPs (four kappa and one lambda **immunoglobulin light chains**) were used in this assay that demonstrated these proteins bound THP with different affinity. BJPs competed among themselves for binding to THP. The binding site was a **peptide** portion of THP since these proteins also bound deglycosylated THP. Also, one monoclonal antibody directed against a **peptide** segment of human THP prevented binding of THP to BJPs. By altering the conformation of THP, reducing agents decreased binding between these two proteins in concentration-dependent fashion. In turbidity studies, the monoclonal antibody that prevented binding and a reducing agent, dithiothreitol, decreased coaggregation. Deglycosylated THP did not coaggregate with BJPs. We concluded that ionic interaction between BJPs and a specific **peptide** binding site on THP promoted heterotypic coaggregation. The carbohydrate moiety of THP was also essential for coaggregation, perhaps by facilitating homotypic aggregation of THP.

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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 09:15:25 ON 17 JUN 2002
L1 463 S UROMODULIN
L2 47 S L1 AND PEPTIDE
L3 1 S L2 AND IMMUNOGLOBULIN LIGHT CHAIN

=> dup remove l2
PROCESSING COMPLETED FOR L2
L4 20 DUP REMOVE L2 (27 DUPLICATES REMOVED)

=> d l4 1-20 cbib abs

L4 ANSWER 1 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)
2002:470599 The Genuine Article (R) Number: 555YA. Vitamin A excreted in the urine of canines is associated with a Tamm-Horsfall like protein. Schweigert F J (Reprint); Raila J; Haebel S. Univ Potsdam, Inst Nutr Sci, Arthur Scheunert Allee 114-116, D-14558 Potsdam, Germany (Reprint); Univ Potsdam, Inst Nutr Sci, D-14558 Potsdam, Germany; Univ Potsdam, Interdisciplinary Res Ctr Biopolymers, D-14476 Golm, Germany. VETERINARY RESEARCH (MAY-JUN 2002) Vol. 33, No. 3, pp. 299-311. Publisher: E D P SCIENCES. 7, AVE DU HOGGAR, PARC D ACTIVITES COURTABOEUF, BP 112, F-91944 LES ULIS CEDEXA, FRANCE. ISSN: 0928-4249. Pub. country: Germany. Language:

English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Under physiological conditions canines transport vitamin A in blood plasma primarily as retinyl esters bound to lipoproteins and excrete substantial amounts of vitamin A as retinol and retinyl esters with urine. In the aqueous environment of urine, the hydrophobic vitamin A has to be associated with a protein. This vitamin A-protein complex was purified to homogeneity, prepared by preparative ultracentrifugation (density 1.21 g/mL), native polyacrylamide gel electrophoresis (PAGE) and size exclusion chromatography. The vitamin A-protein complex has a high molecular mass of > 5 000 kDa under native conditions. SDS PAGE under reduced conditions revealed a single band with a molecular mass of about 100 kDa for the protein moiety. **Peptides** obtained after limited proteolysis with trypsin from the 100 kDa protein were characterised by MALDI-TOF mass spectrometry and showed amino acid sequence homology to the human Tamm-Horsfall Protein (THP). This was further confirmed by a positive immunoreaction of the isolated protein with crossreacting human THP antibodies. The localisation of THP in dog kidneys was determined by using immunohistology. The reaction was strong along the entire thick ascending limb of the Henle loop and distal convoluted tubule. Our data point to the possibility that THP functions as a novel carrier for vitamin A in the urine of canines.

L4 ANSWER 2 OF 20 MEDLINE

2002317384 Document Number: 22054966. PubMed ID: 12060070. Identification and characterization of a unique Xenopus laevis egg envelope component, ZPD. Lindsay LeAnn L; Yang Joy C; Hedrick Jerry L. (Section of Molecular and Cellular Biology, University of California, Davis, California 95616, USA.) DEVELOPMENT GROWTH AND DIFFERENTIATION, (2002 Jun) 44 (3) 205-12. Journal code: 0356504. ISSN: 0012-1592. Pub. country: Japan. Language: English.

AB We report the identification of a previously undetected Xenopus laevis egg envelope component discovered through cloning experiments. A cDNA sequence was found that represented a mature protein of 32 kDa. **Peptide** antibodies were generated to probe for the protein in egg envelope samples and reactivity was found to a glycoprotein of approximately 80 kDa. When deglycosylated egg envelope samples were probed, a 32 kDa protein was labeled, confirming the size of the translated cDNA sequence. A BLAST analysis showed that it is most closely related (34% amino acid identity) to the ZP domains of mammalian tectorin, **uromodulin** and ZPA. From a dendrogram of known egg envelope glycoproteins, the new glycoprotein was shown to be unique among egg envelope components and was designated ZPD. A similar glycoprotein was identified by immunocrossreactivity in Xenopus tropicalis and Xenopus borealis egg envelopes.

L4 ANSWER 3 OF 20 MEDLINE DUPLICATE 1

2001700801 Document Number: 21616969. PubMed ID: 11741296. Analysis of the C-terminal structure of urinary Tamm-Horsfall protein reveals that the release of the glycosyl phosphatidylinositol-anchored counterpart from the kidney occurs by phenylalanine-specific proteolysis. Fukuoka S; Kobayashi K. (Graduate School of Agriculture, Kyoto University, 611-0011 Uji, Kyoto, Japan.. fukuoka@food2.food.kyoto-u.ac.jp) . BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2001 Dec 21) 289 (5) 1044-8. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB Tamm-Horsfall protein (THP), also known as **uromodulin**, is a major glycoprotein synthesized in the kidney. THP is expressed on the luminal surface of the membrane with the glycosyl phosphatidylinositol (GPI) anchor and excreted in urine at a rate of 50-100 mg per day. Although THP is the most abundant urinary protein, the function of THP remains unclear. In addition, little is known about the mechanism by which large amounts of THP are actively released into the urinary fluid. In this study, we examined the C-terminal structure of highly purified THP derived

from human urine. Carboxypeptidase Y efficiently degraded urinary THP, indicating that the C-terminal structure of the protein contains an amino acid residue with a free carboxyl moiety. These results are consistent with our previous finding that urinary THP does not bind anti-CRD antibody. We obtained **peptides** from the complete digestion of urinary THP with lysylendopeptidase. We purified the most C-terminal **peptide** with p-phenylene diisothiocyanate-controlled pore glass (DITC-CPG) beads. N-terminal sequence analysis indicated the **peptide** begins with Tyr 520 and ends between E539 and E576. Direct C-terminal amino acid sequencing of highly purified urinary THP gave a sequence of -X-(Q)-G-(R)-F, corresponding to amino acids 544-548, -S-Q-G-R-F. We therefore conclude that urinary THP is generated by a proteolytic cleavage between F548 and S549, 66 amino acids upstream of a possible GPI-anchor attachment site. Because the sequence of THP, including the cleavage site, is highly homologous to that of GP2, a GPI-anchored protein within the pancreas, and both THP and GP2 are abundantly found as soluble forms in the excreted fluids, a common mechanism may exist governing the proteolytic release of GPI-anchored membrane proteins.

L4 ANSWER 4 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)

2002:267182 The Genuine Article (R) Number: 531ZA. Functional significance of IL-2 carbohydrate recognition. Fukushima K (Reprint); Yamashita K. Sasaki Inst, Dept Biochem, Chiyoda Ku, Tokyo 1010062, Japan. TRENDS IN GLYCOSCIENCE AND GLYCOTECHNOLOGY (NOV 2001) Vol. 13, No. 74, pp. 595-602. Publisher: FCCA-FORUM CARBOHYDRATES COMING AGE. C/O GAKUSHIN PUBLISHING CO LTD 1-1-8 TARUMI-CHO, SUITA 564-0062, OSAKA, 30015, JAPAN. ISSN: 0915-7352 . Pub. country: Japan. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Some cytokines have a carbohydrate recognition activity which seems to modulate the interaction between cytokines and their receptors in an immune system. In this article, we have given an overview of the studies on cytokine's carbohydrate recognition activity and reviewed the functional roles of IL-2 carbohydrate recognition activity, CTLL-2 cells proliferate dependently on IL-2. Since a high-mannose type glycan with five or six mannosyl residues can inhibit IL-2-dependent cell proliferation and its signal transduction, it was indicated that the high-mannose type glycan functioned as a modulator of IL-2 on T cell proliferation. Since it has been reported that each IL-2 receptor subunit expressed independently shows only weak binding to IL-2, the mechanism by which IL-2 stimulates the formation of a high affinity IL-2-IL-2Ralpha, -beta, or -gamma complex remained unclear. However, we found that IL-2 recognizes both the high-mannose type glycan with five or six mannosyl residues on IL-2 receptor alpha subunit and its specific **peptide** sequence. The formation of IL-2-IL-2Ralpha complex via dual recognition may be a trigger to form the high-affinity receptor complex which consists of all constituents required for the cellular signaling.

L4 ANSWER 5 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)

1999:797912 The Genuine Article (R) Number: 246AM. The lectin-like domain of tumor necrosis factor-alpha increases membrane conductance in microvascular endothelial cells and peritoneal macrophages. Hribar M; Bloc A; vanderGoot F G; Fransen L; DeBaetselier P; Grau G E; Bluethmann H; Matthay M A; Dunant Y; Pugin J; Lucas R (Reprint). UNIV GENEVA, DEPT PHARMACOL, 1 RUE MICHEL SERVET, CH-1211 GENEVA 14, SWITZERLAND (Reprint); UNIV GENEVA, DEPT PHARMACOL, CH-1211 GENEVA 14, SWITZERLAND; UNIV GENEVA, DEPT INTERNAL MED, DIV MED INTENS CARE, GENEVA, SWITZERLAND; UNIV GENEVA, DEPT BIOCHEM, CH-1211 GENEVA 4, SWITZERLAND; INNOGENET, GHENT, BELGIUM; UNIV BRUSSELS, CELLULAR IMMUNOL LAB, BRUSSELS, BELGIUM; UNIV MEDITERRANEE, UNITE RICKETTS, MARSEILLE, FRANCE; HOFFMANN LA ROCHE AG, DEPT ROCHE GENET, BASEL, SWITZERLAND; CARDIOVASC RES INST, SAN FRANCISCO, CA. EUROPEAN JOURNAL OF IMMUNOLOGY (OCT 1999) Vol. 29, No. 10, pp. 3105-3111. Publisher: WILEY-V C H VERLAG GMBH. MUHLENSTRASSE 33-34, D-13187 BERLIN,

GERMANY. ISSN: 0014-2980. Pub. country: SWITZERLAND; BELGIUM; FRANCE; USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Herein, we show that TNF exerts a pH-dependent increase in membrane conductance in primary lung microvascular endothelial cells and peritoneal macrophages. This effect was TNF receptor-independent, since it also occurred in cells isolated from mice deficient in both types of TNF receptors. A TNF mutant in which the three amino acids critical for the lectinlike activity were replaced by an alanine did not show any significant effect on membrane conductance. Moreover, a synthetic 17-amino acid **peptide** of TNF, which was previously shown to exert lectin-like activity, also increased the ion permeability in these cells. The amiloride sensitivity of the observed activity suggests a binding of TNF to an endogenous ion channel rather than channel formation by TNF itself. This may have important implications in mechanisms of TNF-mediated vascular pathology.

L4 ANSWER 6 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)

1999:838574 The Genuine Article (R) Number: 250GX. Membrane interaction of TNF is not sufficient to trigger increase in membrane conductance in mammalian cells. vanderGoot F G (Reprint); Pugin J; Hribar M; Fransen L; Dunant Y; DeBaetselier P; Bloc A; Lucas R. UNIV GENEVA, DEPT BIOCHEM, QUAI ERNEST ANSERMET, CH-1211 GENEVA, SWITZERLAND (Reprint); UNIV GENEVA, DIV MED INTENS CARE, CH-1211 GENEVA, SWITZERLAND; UNIV GENEVA, DEPT PHARMACOL, CH-1211 GENEVA, SWITZERLAND; INNOGENETICS, GHENT, BELGIUM; FREE UNIV BRUSSELS, VIB, BRUSSELS, BELGIUM. FEBS LETTERS (22 OCT 1999) Vol. 460, No. 1, pp. 107-111. Publisher: ELSEVIER SCIENCE BV. PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. ISSN: 0014-5793. Pub. country: SWITZERLAND; BELGIUM. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Tumor necrosis factor (TNF) can trigger increases in membrane conductance of mammalian cells in a receptor-independent manner via its lectin-like domain. A lectin-deficient TNF mutant, lacking this activity, was able to bind to artificial liposomes in a pH-dependent manner, but not to insert into the bilayer, just like wild type TNF, A **peptide** mimicking the lectinlike domain, which can still trigger increases in membrane currents in cells, failed to interact with liposomes, Thus, the capacity of TNF to trigger increases in membrane conductance in mammalian cells does not correlate with its ability to interact with membranes, suggesting that the cytokine does not form channels itself, but rather interacts with endogenous ion channels or with plasma membrane proteins that are coupled to ion channels, (C) 1999 Federation of European Biochemical Societies.

L4 ANSWER 7 OF 20 MEDLINE DUPLICATE 2

97432121 Document Number: 97432121. PubMed ID: 9286085. Mapping of **peptides** and protein fragments in human urine using liquid chromatography-mass spectrometry. Heine G; Raida M; Forssmann W G. (Lower Saxony Institute for Peptide Research, Hannover, Germany.) JOURNAL OF CHROMATOGRAPHY. A, (1997 Jul 25) 776 (1) 117-24. Journal code: 9318488. Pub. country: Netherlands. Language: English.

AB A method for the mapping of **peptide** mixtures, heterogeneous with respect to the concentration and the size of individual **peptides**, was established with the aim of obtaining a comprehensive analysis of human urine **peptides**. **Peptide** extraction and fractionation were optimized to achieve a two-step analysis, using reversed-phase and ion-exchange chromatography. Highly sensitive detection of **peptides** was performed by coupling microbore HPLC with electrospray mass spectrometry (ESI-MS). **Peptides** such as urodilatin, angiotensin and fragments of psoriasin, granulin and **uromodulin** were isolated and sequenced. The procedure presented here is a tool for the analysis of complex **peptide** mixtures from human urine.

L4 ANSWER 8 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)
95:279380 The Genuine Article (R) Number: QU091. MOLECULAR-CLONING OF CHICK BETA-TECTORIN, AN EXTRACELLULAR-MATRIX MOLECULE OF THE INNER-EAR. KILLICK R; LEGAN P K; MALENCZAK C; RICHARDSON G P (Reprint). UNIV SUSSEX, SCH BIOL SCI, BRIGHTON BN1 9QG, E SUSSEX, ENGLAND (Reprint); UNIV SUSSEX, SCH BIOL SCI, BRIGHTON BN1 9QG, E SUSSEX, ENGLAND. JOURNAL OF CELL BIOLOGY (APR 1995) Vol. 129, No. 2, pp. 535-547. ISSN: 0021-9525. Pub. country: ENGLAND . Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The tectorial membrane is an extracellular matrix lying over the apical surface of the auditory epithelium. Immunofluorescence studies have suggested that some proteins of the avian tectorial membrane, the tectorins, may be unique to the inner ear (Killick, R., C. Malenczak, and G. P. Richardson. 1992. Hearing Res. 64:21-38). The cDNA and deduced amino acid sequences for chick beta-tectorin are presented. The cDNA encodes a protein of 36,902.6 D with a putative signal sequence, four potential N-glycosylation sites, 13 cysteines, and a hydrophobic COOH terminus. Western blots of two-dimensional gels using antibodies to a synthetic **peptide** confirm the identity of the cDNA. Southern and Northern analysis suggests that beta-tectorin is a single-copy gene only expressed in the inner ear. The predicted COOH terminus is similar to that of glycosylphosphatidylinositol-linked proteins, and antisera raised to this region react with in vitro translation products of the cDNA clone but not with mature beta-tectorin. These data suggest beta-tectorin is synthesized as a glycosylphosphatidylinositol-linked precursor, targeted to the apical surface of the sensory epithelium by the lipid moiety, and then further processed. Sequence analysis indicates the predicted protein possesses a zona pellucida domain, a sequence that is common to a limited number of other matrix-forming proteins and may be involved in the formation of filaments. In the cochlear duct, beta-tectorin is expressed in the basilar papilla, in the clear cells and the cuboidal cells, as well as in the striolar region of the lagena macula. The expression of beta-tectorin is associated with hair cells that have an apical cell surface specialization known as the 275-kD hair cell antigen restricted to the basal region of the hair bundle, suggesting that matrices containing beta-tectorin are required to drive this hair cell type.

L4 ANSWER 9 OF 20 MEDLINE DUPLICATE 3
95178555 Document Number: 95178555. PubMed ID: 7873609. Nucleotide sequence and **peptide** motifs of mouse **uromodulin** (Tamm-Horsfall protein)--the most abundant protein in mammalian urine. Prasadan K; Bates J; Badgett A; Dell M; Sukhatme V; Yu H; Kumar S. (Warren Medical Research Institute, University of Oklahoma Health Sciences Center, Oklahoma City 73104.) BIOCHIMICA ET BIOPHYSICA ACTA, (1995 Feb 21) 1260 (3) 328-32. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB The mouse **uromodulin** cDNA sequence was sequenced. The predicted **peptide** sequence is 642 amino acids long and contains several modular components including four epidermal growth factor like repeats, one betaglycan-like domain (ZP domain), and a consensus sequence for attachment of a glycosyl-phosphatidyl-inositol anchor. An arginine-glycine-aspartate tripeptide reported for rat and human sequence is absent in the mouse. There are several potential sites for post-translational modification.

L4 ANSWER 10 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)
95:690785 The Genuine Article (R) Number: RX093. SURFACE-ANTIGENS IN RENAL-CARCINOMA - PRESENTATION OF MHC I-RESTRICTED SELF **PEPTIDES** . STEVANOVIC S (Reprint); POMER S; RAMMENSEE H G. DEUTSCH KREBSFORSCHUNGSZENTRUM, TUMORVIRUS IMMUNOL ABT 0620, NEUENHEIMER FELD 242, D-69120 HEIDELBERG, GERMANY (Reprint). AKTUELLE UROLOGIE (SEP 1995) Vol. 26, Sp. iss. 1, pp. 45-46. ISSN: 0001-7868. Pub. country: GERMANY.

Language: German.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB MHC I-restricted self **peptides** were isolated from a series of renal carcinoma tissue samples, and compared to **peptides** isolated from healthy kidney tissue. In most of the tumor tissues MHC I-restricted **peptide** presentation was not dimished if compared to autologous kidney, i.e. there was no loss or down-regulation of HLA molecules. Two of eleven **peptides** characterized so far were presented by kidney as well as by tumor cells (fragments of MHC II or actin), while the other **peptides** characterized (fragments of histone, vimentin, **uromodulin**, and other proteins) were only found in either of the tissues. Both undiminished presentation and different presentation patterns are prerequisites for developing a **peptide**-specific immune therapy.

L4 ANSWER 11 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)
94:688759 The Genuine Article (R) Number: PN101. CONJUGATES OF CARBOHYDRATE CHAINS OF ALPHA(1)-ACID GLYCOPROTEIN WITH POLYACRYLAMIDE RETAIN THE IMMUNOMODULATING ACTIVITY. SHIYAN S D (Reprint); PUHALSKY A L; TOPTIGINA A P; NASONOV V V; BOVIN N V. RUSSIAN ACAD SCI, MM SHEMYAKIN & YA OVCHINNIKOV INST BIOORGAN CHEM, UL MIKLUKHO MAKLAYA 16-10, MOSCOW 117871, RUSSIA (Reprint); RUSSIAN ACAD MED SCI, CTR MED GENET, MOSCOW, RUSSIA. BIOORGANICHESKAYA KHIMIYA (AUG/SEP 1994) Vol. 20, No. 8-9, pp. 994-1000. ISSN: 0132-3423. Pub. country: RUSSIA. Language: Russian.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Translocation of carbohydrate glycoprotein N-chains onto soluble polyacrylamide was proposed as a method for studying the biological role of carbohydrate chains. N-linked carbohydrate chains of alpha1-acid glycoprotein (AGP) were aminated at the reducing GlcNAc moiety and covalently attached to polyacrylamide (PAA). Thus ''pseudo-AGP'' was obtained where **peptide** core was replaced with PAA. The synthetic model mimics AGP by M(r) and carbohydrate content as well as the ratio of tetra-, tri- and diantennary and mono-, di-, tri- and tetrasialo chains. It was shown that the conjugate inhibits proliferation of lymphocytes like the parent AGP. Therefore, the property of AGP to inhibit the lymphocyte proliferation is attributed to its carbohydrate chains, whereas **peptide** core serves as carrier providing polyvalent interaction of multiple carbohydrate chains with cell.

L4 ANSWER 12 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)
94:70667 The Genuine Article (R) Number: MV866. MAPPING THE LECTIN-LIKE ACTIVITY OF TUMOR-NECROSIS-FACTOR. LUCAS R (Reprint); MAGEZ S; DELEYS R; FRANSEN L; SCHEERLINCK J P; RAMPELBERG M; SABLON E; DEBAETSELIER P. VRIJE UNIV BRUSSELS, CELLULAR IMMUNOL LAB, CAMPUS RODE, PAARDENSTR 65, B-1640 RHODE ST GENESE, BELGIUM (Reprint); VRIJE UNIV BRUSSELS, GEN BIOL LAB, B-1640 RHODE ST GENESE, BELGIUM; INNOGENET NV, B-9052 ZWIJNAARDE, BELGIUM. SCIENCE (11 FEB 1994) Vol. 263, No. 5148, pp. 814-817. ISSN: 0036-8075. Pub. country: BELGIUM. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Tumor necrosis factor (TNF), but not lymphotoxin (LT), is directly trypanolytic for salivarian trypanosomes. This activity was not blocked by soluble 55-kilodalton and 75-kilodalton TNF receptors, but was potently inhibited by N,N'-diacetylchitobiose, an oligosaccharide that binds TNF. Comparative sequence analysis of TNF and LT localized the trypanocidal region, and synthetic **peptides** were trypanolytic. TNF molecules in which the trypanocidal region was mutated or deleted retained tumoricidal activity. Thus, trypanosome-TNF interactions occur via a TNF domain, probably with lectin-like affinity, which is functionally and spatially distinct from the mammalian TNF receptor binding sites.

L4 ANSWER 13 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1994:518474 Document No.: PREV199497531474. Nucleotide sequence and **peptide** motifs of mouse Tamm-Horsfall protein: The most abundant

protein in mammalian urine. Prasadan, Krishna (1); Bates, James (1); Badgett, Allen (1); Dell, Maria (1); Sukhatme, Vikas; Yu, Heron; Kumar, Satish (1). (1) Warren Med. Res. Inst., Univ. Okla. Health Sci. Cent., Oklahoma City, OK USA. Journal of the American Society of Nephrology, (1994) Vol. 5, No. 3, pp. 668. Meeting Info.: Abstracts Submitted for the 27th Annual Meeting of the American Society of Nephrology Orlando, Florida, USA October 26-29, 1994 ISSN: 1046-6673. Language: English.

L4 ANSWER 14 OF 20 MEDLINE DUPLICATE 4
94220097 Document Number: 94220097. PubMed ID: 7513160.
Uromodulin (Tamm-Horsfall protein) is a leukocyte adhesion molecule. Toma G; Bates J M Jr; Kumar S. (W.K. Warren Medical Research Institute, University of Oklahoma Health Sciences Center, Oklahoma City 73104.) BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1994 Apr 15) 200 (1) 275-82. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.
AB **Uromodulin** (Tamm-Horsfall protein), the most abundant constituent of human urine, is synthesized exclusively in the kidney tubular epithelium and its amino acid sequence suggests a capacity for cell adhesion. We investigated adhesion between human **uromodulin** and neutrophils by allowing **uromodulin**, immobilized on microtiter plates, to interact with neutrophils. It was found that neutrophils attached to **uromodulin** in a saturable manner. The binding was inhibited by **uromodulin** in solution. It required metabolically active cells, was calcium sensitive and could be inhibited by arginine-glycine- aspartate-containing **peptides** in solution. These data suggest that uromodoulin can act as a specific ligand for neutrophils. This interaction is potentially important in leukocyte trafficking in the kidney and in the pathogenesis of interstitial nephritis.

L4 ANSWER 15 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)
93:749146 The Genuine Article (R) Number: ML643. BENCE-JONES PROTEINS BIND TO A COMMON **PEPTIDE** SEGMENT OF TAMM-HORSFALL GLYCOPROTEIN TO PROMOTE HETEROTYPIC AGGREGATION. HUANG Z Q; KIRK K A; CONNELLY K G; SANDERS P W (Reprint). UNIV ALABAMA, DEPT MED, DIV NEPHROL, CTR NEPHROL RES & TRAINING, 642 LYONS HARRISON RES BLDG, BIRMINGHAM, AL, 35292; UNIV ALABAMA, DEPT PHYSIOL, DIV NEPHROL, CTR NEPHROL RES & TRAINING, BIRMINGHAM, AL, 35292; UNIV ALABAMA, DEPT BIOSTAT & BIOMATH, DIV NEPHROL, CTR NEPHROL RES & TRAINING, BIRMINGHAM, AL, 35292; VET AFFAIRS MED CTR, BIRMINGHAM, AL, 35292. JOURNAL OF CLINICAL INVESTIGATION (DEC 1993) Vol. 92, No. 6, pp. 2975-2983. ISSN: 0021-9738. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Bence Jones proteins (BJPs) are the major pathogenic factor causing cast nephropathy (''myeloma kidney'') by coaggregation with Tamm-Horsfall glycoprotein (THP). Understanding the interaction between these proteins is therefore important in developing treatment strategies to prevent renal failure from cast formation in multiple myeloma. We developed an enzyme-linked immunoassay to examine this phenomenon. Five different human BJPs (four kappa and one lambda immunoglobulin light chains) were used in this assay that demonstrated these proteins bound THP with different affinity. BJPs competed among themselves for binding to THP. The binding site was a **peptide** portion of THP since these proteins also bound deglycosylated THP. Also, one monoclonal antibody directed against a **peptide** segment of human THP prevented binding of THP to BJPs. By altering the conformation of THP, reducing agents decreased binding between these two proteins in concentration-dependent fashion. In turbidity studies, the monoclonal antibody that prevented binding and a reducing agent, dithiothreitol, decreased coaggregation. Deglycosylated THP did not coaggregate with BJPs. We concluded that ionic interaction between BJPs and a specific **peptide** binding site on THP promoted heterotypic coaggregation. The carbohydrate moiety of THP was also

essential for coaggregation, perhaps by facilitating homotypic aggregation of THP.

L4 ANSWER 16 OF 20 MEDLINE DUPLICATE 5

93286182 Document Number: 93286182. PubMed ID: 8509450. A GPI-anchored sea urchin sperm membrane protein containing EGF domains is related to human **uromodulin**. Mendoza L M; Nishioka D; Vacquier V D. (Center for Marine Biotechnology and Biomedicine, Scripps Institution of Oceanography, University of California, San Diego, La Jolla 92093-0202.) JOURNAL OF CELL BIOLOGY, (1993 Jun) 121 (6) 1291-7. Journal code: 0375356. ISSN: 0021-9525. Pub. country: United States. Language: English.

AB An Mr 63-kD sea urchin sperm flagellar membrane protein has been previously implicated as a possible receptor for egg jelly ligand(s) that trigger the sperm acrosome reaction (AR). The cDNA and deduced amino acid sequences of the 63-kD protein are presented. The open reading frame codes for a protein of 470 amino acids which contains a putative signal sequence of 25 residues. Western blots using antibodies to two synthetic **peptides** confirm the sequence to be that of the 63-kD protein. The mRNA is approximately 2,300 bases in length and the gene appears to be single copy. The protein is released from sperm membrane vesicles by treatment with phosphatidylinositol-specific phospholipase C, showing that it is anchored to the flagellar membrane by glycosylphosphatidyl inositol (GPI). Although we cannot demonstrate involvement of the 63-kD protein in the AR, it is of potential interest because it shares significant similarity with the developmentally expressed proteins crumbs, notch and xotch as well as human **uromodulin** over a region that includes two separate EGF repeats.

L4 ANSWER 17 OF 20 MEDLINE DUPLICATE 6

93311995 Document Number: 93311995. PubMed ID: 8323280. N-linked sugar chain structure of recombinant human lymphotoxin produced by CHO cells: the functional role of carbohydrate as to its lectin-like character and clearance velocity. Fukushima K; Watanabe H; Takeo K; Nomura M; Asahi T; Yamashita K. (Department of Biochemistry, Sasaki Institute, Tokyo, Japan.) ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (1993 Jul) 304 (1) 144-53. Journal code: 0372430. ISSN: 0003-9861. Pub. country: United States. Language: English.

AB Recombinant human lymphotoxin (rhLT) produced by CHO cells transfected with human LT genomic DNA was purified to homogeneity, but approximately 5% of the molecules were devoid of the last two amino terminal residues. A **peptide** N-glycosylated at Asn62 (Tr-45) and one partially O-glycosylated at Thr7 (Tr-14) on cleavage with trypsin were separated by reverse phase HPLC. The N-linked sugar chains of Tr-45 were released quantitatively as oligosaccharides on hydrazinolysis (100 degrees C, 8 h), followed by N-acetylation. After being reduced with either NaB3H4 or NaB2H4, their structures were determined by a combination of serial lectin affinity chromatography, exoglycosidase digestion, and methylation analysis: 82.7% of the sugar chains occur as biantennary complex-type sugar chains, the remainder being C-2 and C-2,4/C-2,6 branched triantennary, and C-2,4 and C-2,6 branched tetraantennary complex-type sugar chains with a fucosylated mannose core. Their sialic acid residues occur only as the Neu5Ac alpha 2-->3Gal group. The clearance velocity from the bloodstream dramatically increased with desialylation, and rhLT tends to have accumulated in the kidney, indicating that there may exist other mechanisms for clearance from the circulation besides the galactose-binding protein in hepatocytes and the filtration system of the kidney. Desialylated rhLT showed a lectin-like binding character to **uromodulin** similar to that of tumor necrosis factor, although intact rhLT did not. The interaction between desialylated rhLT and **uromodulin** was inhibited by N,N'-diacetylchitobiose and [Man alpha 1-->6(Man alpha 1-->3)Man alpha 1-->6](Man alpha 1-->2Man alpha 1-->3)Man beta 1-->4GlcNAc beta 1-->4GlcNAc-->Asn. These results indicate that the lectin-like domain of rhLT is exposed on its desialylation.

L4 ANSWER 18 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)
92:662319 The Genuine Article (R) Number: JX223. THE ASN-LINKED CARBOHYDRATE CHAINS OF HUMAN TAMM-HORSFALL GLYCOPROTEIN OF ONE MALE - NOVEL SULFATED AND NOVEL N-ACETYLGALACTOSAMINE-CONTAINING N-LINKED CARBOHYDRATE CHAINS. HARD K; VANZADELHOFF G; MOONEN P; KAMERLING J P; VLIEGENTHART J F G (Reprint). UNIV UTRECHT, CTR BIJVOET, DEPT BIOORGAN CHEM, POB 80075, 3508 TB UTRECHT, NETHERLANDS. EUROPEAN JOURNAL OF BIOCHEMISTRY (01 NOV 1992) Vol. 209, No. 3, pp. 895-915. ISSN: 0014-2956. Pub. country: NETHERLANDS. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Human Tamm-Horsfall glycoprotein has been purified from the urine of one male. The Asn-linked carbohydrate chains were enzymically released by **peptide**-N4-(N-acetyl-beta-glucosaminyl)asparagine amidase F, and separated from the remaining protein by gel-permeation chromatography on Bio-Gel P-100. Fractionation of the intact (sulfated) sialylated carbohydrate chains was achieved by a combination of three liquid-chromatographic techniques, namely, anion-exchange FPLC on Q-Sepharose, amine-adsorption HPLC on Lichrospher-NH2, and high-pH anion-exchange chromatography on CarboPac PA1. In total, more than 150 carbohydrate-containing fractions were obtained, some of which still contained mixtures of oligosaccharides. The primary structure of 30 N-glycans, including 10 novel oligosaccharides, were determined by one- and two-dimensional H-1-NMR spectroscopy at 500 MHz or 600 MHz. The types of compounds identified range from non-fucosylated, monosialylated, diantennary to fucosylated, tetrasialylated, tetraantennary carbohydrate chains, possessing the following terminal structural elements:
[GRAPHICS]
The largest GalNAc-containing compound has the following structure:( )[GRAPHICS]

L4 ANSWER 19 OF 20 MEDLINE DUPLICATE 7
93042872 Document Number: 93042872. PubMed ID: 1384752. T-lymphocyte control of HLA-DR blood monocyte differentiation into neo-fibroblasts. Further evidence of pluripotential secreting functions of HLA-DR monocytes, involving not only collagen but also **uromodulin**, amyloid-beta **peptide**, alpha-fetoprotein and carcinoembryonic antigen. Bringuier A F; Seebold-Choqueux C; Moricard Y; Simmons D J; Milhaud G; Labat M L. (CNRS URA 163, Centre de Recherches Biomedicales des Cordeliers, Laboratoire de Physiopathologie Osseuse-Retrovirologie, Paris, France.) BIOMEDICINE AND PHARMACOTHERAPY, (1992) 46 (2-3) 91-108. Journal code: 8213295. ISSN: 0753-3322. Pub. country: France. Language: English.

AB Previous studies led us to demonstrate in pathological situations that the fibroblast, not the macrophage, was the terminal maturation step of the HLA-DR monocyte and that the entire process came under T-lymphocyte control. Fibrosis which developed under immunosuppressive treatment (cyclosporin) after organ transplantation is an illustration of these in vitro observations. The present in vitro study was undertaken in order to investigate whether or not this transformation process takes place under physiological conditions and if so, the nature of the T-lymphocyte control. We report that normal HLA-DR monocytes/macrophages are able to secrete type 1 collagen and to differentiate into neo-fibroblasts. However, contrarily to what happened in pathology, only a few neo-fibroblasts developed transiently. The addition of conditioned medium (CM) from activated T-lymphocytes greatly enhanced the transformation process. Counteracting this CM effect, cell-to-cell contact between neo-fibroblasts and T-cells resulted in the loss of fibroblastic shape. The 'end-result' macrophage engulfed numerous lymphocytes giving rise to a multinucleated cell. This giant cell no longer adhered to the slide and died. The question is raised as to whether the process observed in vitro is involved in vivo in tissue repair. We also report that HLA-DR monocytes and the neo-fibroblasts which derive from them are able to secrete, in

addition to type 1 collagen, a variety of proteins such as **uromodulin**, amyloid-beta **peptide**, alpha-fetoprotein and carcinoembryonic antigen. In cystic fibrosis we previously reported a high level of **uromodulin** production by HLA-DR monocytes differentiating towards the fibroblastic phenotype. Pathologies characterized by excessive production of either alpha-feto-protein, carcinoembryonic antigen, beta-amyloid protein (Alzheimer's disease) should be investigated, taking into account the involvement of HLA-DR monocytes and their possible uncontrolled differentiation into neo-fibroblasts.

L4 ANSWER 20 OF 20 MEDLINE DUPLICATE 8
87177970 Document Number: 87177970. PubMed ID: 3453112. Identification of human **uromodulin** as the Tamm-Horsfall urinary glycoprotein.
Pennica D; Kohr W J; Kuang W J; Glaister D; Aggarwal B B; Chen E Y; Goeddel D V. SCIENCE, (1987 Apr 3) 236 (4797) 83-8. Journal code: 0404511. ISSN: 0036-8075. Pub. country: United States. Language: English.
AB The primary structure of human **uromodulin**, a 616-amino acid, 85-kilodalton glycoprotein with in vitro immunosuppressive properties, was determined through isolation and characterization of complementary DNA and genomic clones. The amino acid sequence encoded by one of the exons of the **uromodulin** gene has homology to the low-density-lipoprotein receptor and the epidermal growth factor precursor. Northern hybridization analyses demonstrate that **uromodulin** is synthesized by the kidney. Evidence is provided that **uromodulin** is identical to the previously characterized Tamm-Horsfall glycoprotein, the most abundant protein in normal human urine.

```
=> s "DIQMTQSPSSLSASLG"
L5            0 "DIQMTQSPSSLSASLG"

=> s  immunoglobulin light chain
L6        14222 IMMUNOGLOBULIN LIGHT CHAIN

=> s l6 and peptide
L7         1525 L6 AND PEPTIDE

=> s l7  and 27 kDa
L8            0 L7 AND 27 KDA

=> s l7 and "27 kDal"
L9            0 L7 AND "27 KDAL"

=> s l7 and soluble
L10          77 L7 AND SOLUBLE

=> dup remove l10
PROCESSING COMPLETED FOR L10
L11           49 DUP REMOVE L10 (28 DUPLICATES REMOVED)

=> s l11 and "27 kilo dalton"
L12           0 L11 AND "27 KILO DALTON"

=> s l11 and mast cell inhibitor
   3 FILES SEARCHED...
L13           0 L11 AND MAST CELL INHIBITOR

=> s mast cell degranulation
   3 FILES SEARCHED...
L14        7366 MAST CELL DEGRANULATION

=> s l14 and inhibitor
```

```
L15       1091 L14 AND INHIBITOR

=> s l15 and peptide
L16        115 L15 AND PEPTIDE

=> s l16 and immunoglobulin
L17         23 L16 AND IMMUNOGLOBULIN

=> s l17 and light chain
L18          1 L17 AND LIGHT CHAIN

=> d l18 cbib abs

L18  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
1994:242521   Document No. 120:242521  Monoclonal and humanized antibodies to
     P-selectin and their therapeutic uses.  Chestnut, Robert W.; Polley,
     Margaret J.; Paulson, James C. (Cytel Corp., USA).  PCT Int. Appl. WO
     9321956 A1 19931111, 80 pp.  DESIGNATED STATES: W:  AT, AU, BB, BG, BR,
     CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL,
     NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US; RW: AT, BE, BF, BJ, CF, CG,
     CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL,
     PT, SE, SN, TD, TG.  (English).  CODEN: PIXXD2.  APPLICATION: WO
     1993-US4274 19930504.  PRIORITY: US 1992-880196 19920505.
AB   The present invention relates to compns. and methods for treating
     inflammation and other pathol. conditions using novel blocking P-selectin
     antibodies which inhibit binding of an antibody secreted by a cell line
     designated ATCC Accession No. HB11041 to P-selectin as measured by a
     competitive inhibition assay.  The antibodies of the invention may be used
     in the treatment of e.g. inflammatory and thrombotic diseases.  Prodn. of
     blocking and nonblocking monoclonal antibodies and humanized antibodies is
     described.  The antibodies of the invention were tested in e.g. treatment
     of acute lung injury, myocardial ischemia and reperfusion, and
     leukocyte-endothelial cell interactions induced by degranulation of tissue
     mast cells.


=> d his

     (FILE 'HOME' ENTERED AT 09:15:13 ON 17 JUN 2002)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 09:15:25 ON
     17 JUN 2002
L1          463 S UROMODULIN
L2           47 S L1 AND PEPTIDE
L3            1 S L2 AND IMMUNOGLOBULIN LIGHT CHAIN
L4           20 DUP REMOVE L2 (27 DUPLICATES REMOVED)
L5            0 S "DIQMTQSPSSLSASLG"
L6        14222 S  IMMUNOGLOBULIN LIGHT CHAIN
L7         1525 S L6 AND PEPTIDE
L8            0 S L7   AND 27 KDA
L9            0 S L7 AND "27 KDAL"
L10          77 S L7 AND SOLUBLE
L11          49 DUP REMOVE L10 (28 DUPLICATES REMOVED)
L12           0 S L11 AND "27 KILO DALTON"
L13           0 S L11 AND MAST CELL INHIBITOR
L14        7366 S MAST CELL DEGRANULATION
L15        1091 S L14 AND INHIBITOR
L16         115 S L15 AND PEPTIDE
L17          23 S L16 AND IMMUNOGLOBULIN
L18           1 S L17 AND LIGHT CHAIN

=> dup remove l17
PROCESSING COMPLETED FOR L17
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L19 17 DUP REMOVE L17 (6 DUPLICATES REMOVED)

=> d l19 1-17 cbib abs

L19 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2002 ACS
2000:911107 Document No. 134:66143 **Peptide** and peptidomimetic anti-allergic agents. Eisenberg, Ronit; Raz, Tamar (Allergene Ltd., Israel). PCT Int. Appl. WO 2000078346 A1 20001228, 63 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-IL346 20000614. PRIORITY: IL 1999-130526 19990617.

AB The invention discloses complex mols. useful as anti-allergic agents. These complex mols. include, in particular, peptidic or peptidomimetic mols. having a first segment which is competent for cell penetration and a second segment which is able to reduce or abolish **mast cell degranulation**, and in particular to reduce or abolish allergy mediators such as histamine secretion from mast cells. Specific examples of **peptides** with the desired activity are disclosed.

L19 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2002 ACS
2000:420987 Document No. 133:57594 Decreasing allergic reactions by inhibition of IgE binding. Caplan, Michael; Sosin, Howard (USA). PCT Int. Appl. WO 2000035484 A2 20000622, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US30238 19991217. PRIORITY: US 1998-216117 19981218.

AB The authors disclose methodol. for preventing allergic response by the inhibition of IgE binding to its epitopes on cognate allergens. Mols. which bind to these epitopes can be identified and synthesized and then formulated to coat or blend with the allergenic components to prevent IgE binding. In one example, the inhibitory mols. are IgE fragments selected using phage display technol. In a second example, the masking reagents are CDR-derived **peptides** or peptidomimetics which bind to the relevant epitopes on the allergens.

L19 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2002 ACS
2000:383954 Document No. 133:26852 Small **peptides** and methods using them for treatment of asthma and inflammation. Houck, John C.; Clagett, James (Histatek, LLC, USA). PCT Int. Appl. WO 2000032217 A1 20000608, 74 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US25583 19981203.

AB Methods for treating allergies, cutaneous inflammation, arthritis, chronic obstruction pulmonary disease and treating chronic inflammatory bowel disease are described. Also described is a method for inhibiting the infiltration of eosinophils into airways of a patient, a method for

inhibiting the mucous release into airways of a patient, a method for blocking IgE activation of a lymphocyte, a method for stabilizing the cell membrane of a lymphocyte, thereby preventing their further involvement in the increased inflammatory response to an IgE antigen challenge, and a method for inhibiting the migration of T-cells. These methods involve administering to the patient a therapeutically effective amt. of a **peptide** having the formula f-Met-Leu-X, (X = Tyr, Tyr-Phe, Phe-Phe, Phe-Tyr).

L19 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2002 ACS

2000:351548 Document No. 132:343308 Bispecific molecules cross-linking immunoreceptor tyrosine-based inhibition motif (ITIM) and immunoreceptor tyrosine-based activation motif (ITAM) for therapy of allergic diseases. Thomas, David; Tam, Sunny (Tanox, Inc., USA). PCT Int. Appl. WO 2000029431 A1 20000525, 31 pp. DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, FI, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US27134 19991116. PRIORITY: US 1998-PV108816 19981117.

AB The invention provides bispecific mols. capable of crosslinking ITAM and ITIM receptors on a cell in order to inhibit cell activation, as well as gene therapy approaches using nucleotides encoding such bispecific mols. for expression in vivo. One example of an ITAM/ITIM receptor pair is Fc.epsilon.RI and HM18, and another is Fc.epsilon.RI and Fc.epsilon.RII. Crosslinking of these receptors with a bispecific mol. of the invention would lead to inhibition of the release of allergic mediators and amelioration of the symptoms of allergic diseases.

L19 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2002 ACS

1999:350603 Document No. 130:347411 Small **peptides** and methods for treatment of asthma and inflammation. Houck, John C. (Hisatek, LLC, USA). PCT Int. Appl. WO 9925372 A1 19990527, 48 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US14103 19980707. PRIORITY: US 1997-65336 19971113.

AB A pharmaceutical compn. is described as an admixt. of a pharmacol. carrier and a **peptide** having the formula f-Met-Leu-X (X = Tyr, Tyr-Phe, Phe-Phe and Phe-Tyr). Also described are methods for inhibiting the degranulation of mast cells and for treating inflammation in a patient, for example, where the inflammation is a result of a disease selected from the group consisting of asthma, rheumatoid arthritis and anaphylaxis. In addn., methods are described for inhibiting the release of cytokines in a patient, for inhibiting the release of histamines in a patient, for inhibiting the release leukotrienes in a patient, for reducing adhesion, migration and aggregation of lymphocytes, eosinophils and neutrophils to a site of inflammation in a patient, for reducing the prodn. of IgE antibodies at site of inflammation in a patient, and for inhibiting increased vascular permeability at site of inflammation in a patient. The methods use the described pharmaceutical compn.

L19 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2002 ACS

1998:426034 Document No. 129:211502 Antiallergic/antiasthmatic activity of oligopeptide related to IgE. Singh, R.; Nath, A.; Gupta, P. P.; Shulka, M.; Khare, S. K.; Kundu, B. (Division of Pharmacology, Central Drug Research Institute, Lucknow, 226001, India). Pharmacological Research,

37(5), 353-356 (English) 1998. CODEN: PHMREP. ISSN: 1043-6618. Publisher: Academic Press Ltd..

AB In spite of continuous research in the field of bronchial asthma, still no satisfactory drug is available. Recently a new class of oligopeptide exhibited antiallergic activity by inhibiting the synthesis of IgE antibody. The analog of ADSDGK (94-335) has shown antiallergic activity in exptl. models. The 94-335 inhibited the passive cutaneous anaphylaxis (PCA) reactions in rats in a dose-dependent manner (0.5-10 mg kg-1 p.o.) by 47-90%. There was a 70-87% protection of **mast cell degranulation** induced by compd. 48/80 with **peptide** 94-335 at 0.5-1.5 mg kg-1 p.o. in rats. This **peptide** also inhibited antigen-induced contraction in sensitized guinea pig ileum. There was 18 and 72% protection to bronchoconstriction induced by histamine and egg albumin, resp., in an aerosol test in guinea pigs. These effects of compd. 94-335 were comparable with that of the clin.-used antiallergic drug disodium cromoglycate (DSCG). The results suggest that **peptide** 94-335 possesses potent antiallergic activity.

L19 ANSWER 7 OF 17 MEDLINE

97477414 Document Number: 97477414. PubMed ID: 9334370. Negative regulation of Fc epsilon RI-mediated degranulation by CD81. Fleming T J; Donnadieu E; Song C H; Laethem F V; Galli S J; Kinet J P. (Department of Pathology, Beth Israel Deaconess Medical Center, Boston, Massachusetts 02215, USA.) JOURNAL OF EXPERIMENTAL MEDICINE, (1997 Oct 20) 186 (8) 1307-14. Journal code: 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.

AB Signaling through the high affinity receptor for **immunoglobulin** E (Fc epsilon RI) results in the coordinate activation of tyrosine kinases before calcium mobilization. Receptors capable of interfering with the signaling of antigen receptors, such as Fc epsilon RI, recruit tyrosine and inositol phosphatases that results in diminished calcium mobilization. Here, we show that antibodies recognizing CD81 inhibit Fc epsilon RI-mediated **mast cell degranulation** but, surprisingly, without affecting aggregation-dependent tyrosine phosphorylation, calcium mobilization, or leukotriene synthesis. Furthermore, CD81 antibodies also inhibit **mast cell degranulation** in vivo as measured by reduced passive cutaneous anaphylaxis responses. These results reveal an unsuspected calcium-independent pathway of antigen receptor regulation, which is accessible to engagement by membrane proteins and on which novel therapeutic approaches to allergic diseases could be based.

L19 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2002 ACS

1996:304300 Document No. 124:333063 **Peptides** for use in treatment of carcinomas. Stanworth, Denis Raymond; Jones, Valerie (Peptide Therapeutics Limited, UK). PCT Int. Appl. WO 9605220 A1 19960222, 20 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-GB1892 19950810. PRIORITY: GB 1994-16316 19940812.

AB The invention provides for the use of compds., particularly a class of **peptides**, which prevent "triggering" of histamine release by **mast cell degranulation** and consequently inhibit carcinoma proliferation. The present invention provides use of a compd. comprising a first neg. charged atom or group and a second neg. charged atom or group, sepd. by a spacing group effective conformationally to position said neg. charged atoms or groups so that they will neutralize the lysine residues of the amino acid sequence Lys Thr Lys at positions 497-499 of the C.epsilon.4 const. domain of human IgE, in the manuf. of a medicament for the treatment of carcinomas, esp. mammary adenocarcinomas.

The present invention provides use of a **peptide** R1mXaa1SpXaa2R2n (I; R1 = a sequence of m amino acids; R2 = a sequence of n amino acids; Xaa1,Xaa2 = neg. charged amino acid, preferably Glu; Sp = spacing residue, preferably a non-charged amino acid, preferably Pro, or a non-charged dipeptide, which provides the spacing required for the neg. charged groups of the Xaa residues to be sufficiently proximal to the lysine residues of the amino acid sequence Lys Thr Lys at positions 497-499 of the C.epsilon.4 const. domain of human IgE to neutralize them; m,n = no. of amino acids in R1 and R2, resp., and each of m and n independently is 0 or an integer 1 - 22, and m + n = 0 - 22; and their terminal functional derivs.) in the manuf. of a medicament for the treatment of carcinomas esp. mammary adenocarcinomas. A representative I compd. is Glu-Pro-Glu.

L19 ANSWER 9 OF 17 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

96094955 EMBASE Document No.: 1996094955. Neutrophil lactoferrin release induced by IgA immune complexes can be mediated either by Fc.alpha. receptors or by complement receptors through different pathways. Zhang W.; Lachmann P.J.. Molecular Immunopathology Unit, MRC Centre, Hills Road,Cambridge CB2 2QH, United Kingdom. Journal of Immunology 156/7 (2599-2606) 1996.
ISSN: 0022-1767. CODEN: JOIMA3. Pub. Country: United States. Language: English. Summary Language: English.

AB Our previous results showed that neutrophil secondary granule release, indicated by release of lactoferrin, was a slow process when induced by IgA immune complexes (IC) formed in heat-inactivated serum, but became very fast if IgA IC were formed in normal human serum. This phenomenon did not apply to the IC of other Ab isotypes. In this paper, we demonstrate that the fast lactoferrin release is caused by complement, mainly due to the deposition of C3b and iC3b on IgA IC. Either CR1 or CR3 can mediate the response and both receptors have to be blocked to prevent it. Complement also influences Fc.alpha.R- mediated lactoferrin release, in that this is enhanced by the anaphylatoxin **peptides**, C5a and C5a(desArg). Divalent cations are required for Fc.alpha.R-and CR3- but not for CR1-mediated lactoferrin release. Genistein, a protein tyrosine kinase **inhibitor**, totally inhibits Fc.alpha.R-mediated response, but has little effect on CR1-mediated response. Therefore, it is clear that different pathways of intracellular signaling are utilized. In addition, stimulation through Fc.alpha.R promotes the receptor up-regulation, which is abolished by the presence of EDTA or genistein.

L19 ANSWER 10 OF 17 MEDLINE DUPLICATE 1

96196877 Document Number: 96196877. PubMed ID: 8612071. Structure based design and characterization of **peptides** that inhibit IgE binding to its high-affinity receptor. McDonnell J M; Beavil A J; Mackay G A; Jameson B A; Korngold R; Gould H J; Sutton B J. (The Randall Institute, King's College London, UK.) NATURE STRUCTURAL BIOLOGY, (1996 May) 3 (5) 419-26. Journal code: 9421566. ISSN: 1072-8368. Pub. country: United States. Language: English.

AB We have designed synthetic **peptide inhibitors** of the interaction between IgE and its high affinity receptor, Fc epsilon RI. The structure of the second domain of CD2 was used as a modelling template for the second alpha-chain domain of Fc epsilon RI, the C-C' loop of which has been implicated in the interaction with IgE. An L-amino acid **peptide** and a retro-enantiomeric D-amino acid **peptide** were designed to mimic the conformation of the C-C' region. Both **peptides** were cyclized by disulphide bond formation between terminal cysteine residues, and show mirror image symmetry by circular dichroism analysis. The C-C' **peptide** mimics act as competitive **inhibitors** of IgE binding. The cyclic L- and retro D-**peptides** exhibited KDs of approximately 3 microM and 11 microM, respectively, for IgE. Further, the **peptides** inhibit IgE-mediated **mast cell degranulation**, an in vitro model of an allergic response.

L19 ANSWER 11 OF 17 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
95227402 EMBASE Document No.: 1995227402. Regulation of integrin-dependent release in human lung mast cells and basophils. Warner J.A.; Goldring K.; Thomas L.H.; Lavens S.E.. Dept. of Physiology and Pharmacology, University of Southampton, Biomedical Sciences Building, Bassett Crescent East,Southampton SO16 7PX, United Kingdom. International Archives of Allergy and Immunology 107/1-3 (151-153) 1995.
ISSN: 1018-2438. CODEN: IAAIEG. Pub. Country: Switzerland. Language: English. Summary Language: English.

AB The interaction of cells with surfaces or components of the extracellular matrix alters cell responses and is regulated by integrins on the cell surface. We have used monoclonal antibodies to CD29 and CD49d followed by an F(ab)2 fragment of rabbit anti-mouse IgG1 to cross-link the integrins on the surface of human lung mast cells and basophils. We found that cross-linking either CD29 or CD49d failed to initiate mediator release from the basophils of non-atopic and atopic donors [histamine release (HR) = 1 .+-. 0.5% for CD29 and 1 .+-. 0.5% for CD49d, n = 10, NS]. In contrast we found that clustering CD29 caused significant HR from the basophils of asthmatic donors (HR = 21 .+-. 5%, n = 10, $p < 0.005$). Clustering of CD49d also caused significant degranulation in the same donors (HR = 9 .+-. 3%, n = 10, $p < 0.11$). Incubating the basophils of these asthmatic donors with a synthetic RGD **peptide** significantly reduced CD29- and CD49d-induced histamine release. CS-1 **peptide** was also found to inhibit CD29-induced histamine release but had no significant effect on CD49d-induced histamine release. The tyrosine kinase **inhibitors**, genistein and piceatannol, completely ablated CD29- and CD49d-induced degranulation. In summary, we have shown that cross-linking integrins can initiate mediator release from the basophils of asthmatic patients and that this appears to involve recognition of RGD and activation of tyrosine kinase.

L19 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2002 ACS
1994:242521 Document No. 120:242521 Monoclonal and humanized antibodies to P-selectin and their therapeutic uses. Chestnut, Robert W.; Polley, Margaret J.; Paulson, James C. (Cytel Corp., USA). PCT Int. Appl. WO 9321956 A1 19931111, 80 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1993-US4274 19930504. PRIORITY: US 1992-880196 19920505.

AB The present invention relates to compns. and methods for treating inflammation and other pathol. conditions using novel blocking P-selectin antibodies which inhibit binding of an antibody secreted by a cell line designated ATCC Accession No. HB11041 to P-selectin as measured by a competitive inhibition assay. The antibodies of the invention may be used in the treatment of e.g. inflammatory and thrombotic diseases. Prodn. of blocking and nonblocking monoclonal antibodies and humanized antibodies is described. The antibodies of the invention were tested in e.g. treatment of acute lung injury, myocardial ischemia and reperfusion, and leukocyte-endothelial cell interactions induced by degranulation of tissue mast cells.

L19 ANSWER 13 OF 17 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
93207014 EMBASE Document No.: 1993207014. Human IgE receptor .alpha.-chain IgG chimera blocks passive cutaneous anaphylaxis reaction in vivo. Haak-Frendscho M.; Ridgway J.; Shields R.; Robbins K.; Gorman C.; Jardieu P.. Promega Corporation,Madison, WI 53711-5399, United States. Journal of Immunology 151/1 (351-358) 1993.
ISSN: 0022-1767. CODEN: JOIMA3. Pub. Country: United States. Language: English. Summary Language: English.

AB Cross-linking of the high affinity IgE receptor (Fc.epsilon.RI) expressed

on mast cells and basophils is essential for triggering anaphylaxis in vivo. Previously, other investigators have tried to produce competitive **inhibitors** using IgE **peptide** analogues and anti-IgE antibodies with limited success. To create a novel specific **inhibitor** of IgE that can block binding of IgE to Fc.epsilon.RI without the capacity to stimulate degranulation, we made an Fc.epsilon.RI-IgG immunoadhesin. The Fc.epsilon.RI-IgG was constructed by gene fusion of the extracellular portion of the human .alpha.-chain of Fc.epsilon.RI, which contains the high affinity binding site for IgE, with a truncated human IgG1 H chain C region. The Fc.epsilon.RI-IgG recognizes both human and murine IgE. Coincubation of Fc.epsilon.RI-IgG with murine IgE prevented sensitization of RBL-2H3 cells and the subsequent histamine release in response to anti-IgE. Similarly, when the Fc.epsilon.RI-IgG was preincubated with equimolar concentrations of either hyperimmune mouse sera or purified mouse IgE, it completely blocked the passive cutaneous anaphylaxis reaction in rats. Furthermore, i.v. administration of Fc.epsilon.RI-IgG following intracutaneous injection of serum from DNP-immunized mice was able to block the passive cutaneous anaphylaxis reaction in a time-dependent fashion. These results demonstrate that Fc.epsilon.RI- IgG is a potent **inhibitor** of IgE binding to intracutaneous mast cells in vivo and may prove clinically useful for the treatment of IgE-mediated disease.

L19 ANSWER 14 OF 17 MEDLINE

93386466 Document Number: 93386466. PubMed ID: 8374754. The effect of intra-articular capsaicin on passive synovial anaphylaxis and blood flow in the rat knee joint. Cambridge H; Brain S D. (Biomedical Sciences Division, King's College, London, UK.) BRAIN RESEARCH, (1993 Aug 6) 618 (2) 238-45. Journal code: 0045503. ISSN: 0006-8993. Pub. country: Netherlands. Language: English.

AB Normal rat and human synovium is innervated by small diameter, unmyelinated, **peptide**-containing nerves. A close anatomical association between these nerves and mast cells has been postulated23, although functional interactions have not been described. Capsaicin is frequently used to activate sensory nerves and we have examined both acute and long-term effects of capsaicin on passive synovial anaphylaxis (PSA) and blood flow in the rat knee joint. The acute injection of capsaicin into the synovial space (330 nmol, 30 min prior to antigen) significantly inhibited plasma extravasation into the joint tissues (measured by accumulation of [125I]-human serum albumin) following PSA, and produced vasoconstriction in normal joints (measured by 133Xe clearance). There was no effect on plasma extravasation when capsaicin was injected 3 h prior to antigen. Inhibition of the PSA response following acute intra-articular capsaicin was not reversed by pretreatment with the cyclo-oxygenase **inhibitor** indomethacin (to inhibit thromboxane generation) or in rats chronically treated with guanethidine (to deplete noradrenaline from post-ganglionic sympathetic fibres). Further, a longer term pre-treatment of the joints with a single intra-articular injection of capsaicin (3.3 mumol) also attenuated plasma extravasation following induction of PSA 7 days later, and was accompanied by a non-significant decrease in joint blood flow. Plasma extravasation in response to compound 48/80, a non-immunological mediator of **mast-cell degranulation**, was not affected in joints treated with capsaicin 7 days previously.(ABSTRACT TRUNCATED AT 250 WORDS)

L19 ANSWER 15 OF 17 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

92238887 EMBASE Document No.: 1992238887. Urticaria and angioedema. Huston D.P.; Bressler R.B.. Baylor College of Medicine, Methodist Hospital, 6565 Fannin,Houston, TX 77030, United States. Medical Clinics of North America 76/4 (805-840) 1992.
ISSN: 0025-7125. CODEN: MCNAA. Pub. Country: United States. Language: English. Summary Language: English.

AB Urticaria and angioedema are usually the clinical consequence of

vasoactive mediators derived from mast cells in the skin or mucosal tissues. Efforts to classify mast cell-mediated causes of urticaria and angioedema have generally been frustrated by their diverse pathogenesis and clinical course. The term acute is typically used to describe fleeting lesions whose recurrence does not extend beyond 6 weeks. Chronic is the term used to describe lesions that persist for more than a few hours but usually less than a day, and recurrences extend for more than 6 weeks. These definitions do not take histology into account. Skin biopsies of fleeting lesions demonstrate a paucity of inflammatory cells, whereas more persistent lesions display a spectrum of perivascular cuffing by predominantly T cells and monocytes. The presence of leukocytoclastic vasculitis in persistent lesions indicates an underlying immune complex disease. Many of the physical urticarias have fleeting lesions that can be induced with the appropriate stimulus for years. This review article has emphasized the clinical course and histology of urticaria and angioedema lesions in an effort to provide a more complete understanding of the pathogenesis and appropriate treatment. Clearly, avoidance of an identifiable inciting stimulus is optimum management, although most patients have no etiology defined or the cause is not realistically avoidable. At present, treatment options for these patients rely on antihistamines to control the immediate consequence of **mast cell degranulation**. Corticosteroids are reserved for the treatment of patients whose urticaria or angioedema lesions persist, reflecting the increasing involvement of mononuclear cells in the disease process. For leukocytoclastic vasculitis, corticosteroids are indicated, and cytotoxic drugs may be required for adequate treatment. Future treatments of urticaria and angioedema will evolve based on elucidation of the relevant cells and soluble mediators and will include counterregulatory or antagonistic **peptides** and drugs. C1 esterase **inhibitor** deficiency is a relatively uncommon cause of angioedema but is important to understand because of its ability to clinically mimic mast cell-mediated angioedemas and its unique pathogenesis and treatment. HAE can be divided into two serologic subtypes that simply reflect the location of the defect in one of the codominantly expressed C1- INH genes on chromosome 11. AAE can be divided into two serologic subtypes. AAE type I is due to massive consumption of C1-INH, presumably by tumor- related immune complexes. AAE type II is due to an anti-C1-INH autoantibody. Acute management of angioedema in any patient with C1-INH deficiency is directed toward maintenance of a patent airway, hemodynamic stability, relief of pain, and identification of causes precipitating the attack. Patients with HAE can be treated prophylactically with attenuated androgens, antifibrinolytic agents, or C1-INH infusions. Although these same agents may be of some benefit in patients with AAE, therapy for these patients is directed toward the underlying disease with AAE type I and immunosuppression with AAE type II. Future approaches to the treatment of C1-INH deficiency will include recombinant C1-INH for passive replacement as well as exploration of the potential for gene therapy.

L19 ANSWER 16 OF 17 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 2

91240042 EMBASE Document No.: 1991240042. Inhibitory effect of tranilast on substance P-induced plasma extravasation in rat skin. Iwamoto I.; Yamazaki H.; Tomioka H.; Yoshida S.. The Second Department of Internal Medicine, Chiba University School of Medicine, Chiba, Japan. Immunopharmacology and Immunotoxicology 13/1-2 (65-71) 1991.
ISSN: 0892-3973. CODEN: IITOEF. Pub. Country: United States. Language: English. Summary Language: English.

AB The effect of tranilast, an **inhibitor** for IgE-mediated mediator release from mast cells, on plasma extravasation induced by the intradermal injection of substance P in rats was examined. Tranilast (100 mg/kg, intraperitoneally) decreased plasma extravasation induced by substance P (10-7-10-5 M). Tranilast decreased plasma extravasation induced by the amino-terminal **peptide** substance P1-9 (10-6-10-4

M), which is active for rat mast cells, but not by the carboxy-terminal **peptide** substance P6-11 (10-6-10-4 M), which is inactive for the mast cells. Therefore, tranilast prevents substance P-induced plasma extravasation most likely by inhibiting **mast cell degranulation**.

L19 ANSWER 17 OF 17 MEDLINE DUPLICATE 3
81190892 Document Number: 81190892. PubMed ID: 7228352. Inhibition of **mast-cell degranulation** by chemotactic **peptides**. Gleisner J M; Ramthun C A; Houck J C. INFLAMMATION, (1981 Mar) 5 (1) 13-7. Journal code: 7600105. ISSN: 0360-3997. Pub. country: United States. Language: English.

AB Pepstatin and f-methionyl **peptides** which are potent chemotactic agents for neutrophils were found to inhibit the increase in vascular permeability of rat skin which follows the injection of 48/80, anti-rat IgE serum, or pulmonary permeability factor. These latter compounds are known to act by releasing histamine from mast cells. f-Met-Leu-Phe, which is the most active chemotactically, was also found to be the most active **inhibitor**.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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